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(54) Title: ANTIDIABETIC AGENTS

(57) Abstract

The instant invention is concerned with aryl and heteroaryl oxyacetic acid type compound which are useful antidiabetic compounds. Compositions and methods for the use of the compounds in the treatment of diabetes and related diseases and for lowering triglyceride levels are also disclosed.

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TITLE OF THE INVENTION
ANTIDIABETIC AGENTS

BACKGROUND OF THE INVENTION

Diabetes refers to a disease process derived from multiple causative factors and characterized by elevated levels of plasma glucose or hyperglycemia. Uncontrolled hyperglycemia is associated with increased and premature mortality due to an increased risk for microvascular and macrovascular disease, including nephropathy, neuropathy, retinopathy, hypertension, stroke, and heart disease. Therefore, glucose homeostasis is critically important for the treatment of diabetes.

Type I diabetes (IDDM) is associated with a deficiency of insulin. Type II, noninsulin dependent diabetes mellitus (NIDDM) is associated with a resistance to the stimulating or regulatory effect of insulin on glucose and lipid metabolism in the main insulin-sensitive tissues, namely, the muscle, liver and adipose tissue. This resistance to to the effect of insulin results in insufficient activation of glucose uptake, oxidation and storage in muscle, inadequate repression of lipolysis in adipose tissue and inadequate supression of glucose production and secretion in liver.

Standard treatments for NIDDM, which have not changed substantially in years, are all associated with limitations. Physical exercise and reduction in calorie intake improves the diabetic condition; however compliance is generally poor. Increasing the plasma level of insulin, either by administering an oral hypoglycemic such as a sulfonylurea (e.g. tolbutamide or glipizide) or by injecting insulin results in insulin levels which are sufficient to stimulate insulin-resistant tissues. However, low levels of plasma glucose and a heightened level of insulin resistance can result.

Thiazolidinediones (glitazones) were suggested to ameliorate many symptoms of NIDDM. These agents increase insulin sensitivity in muscle, liver and adipose tissue in several animal models of NIDDM, hopefully resulting in normaliz d levels of plasma glucose, triglycerides and nonesterified free fatty acids. However, serious undesirable effects have been observed, including cardiac hypertrophy, hemodilution and liver toxicity.

Hyperlipidemia is a condition that is characterized by an abnormally high level of serum lipids. This includes cholesterol, triglycerides and phospholipids. These lipids do not circulate freely in solution in plasma, but are bound to proteins and transported as macromolecular complexes called lipoproteins. See the *Merck Manual*, 16th Ed. 1992 (see for example pp. 1039-1040) and "Structure and Metabolism of Plasma Lipoproteins" in *Metabolic Basis of Inherited Disease*, 6th Ed. 1989, pp. 1129-1138. One form of hyperlipidemia is hypercholesterolemia, which is characterized by elevated LDL cholesterol levels. The initial treatment for hypercholesterolemia is often reduced dietary fat and cholesterol. Coupled with an appropriate exercise regimen, this can be an effective means by which to reduce hyperlipidemia. More typically, this means of lowering hyperlipidemia is insufficient, making drug therapy to reduce serum LDL-cholesterol more appropriate.

Although it is desirable to lower elevated levels of LDL cholesterol, it is also desirable to increase levels of HDL cholesterol, since increased levels of HDL are associated with a reduced risk for coronary heart disease (CHD). See, for example, Gordon, et al., Am. J. Med., *62*, 707-714 (1977); Stampfer, et al., N. England J. Med., *325*, 373-381 (1991); and Kannel, et al., Ann. Internal Med., *90*, 85-91 (1979). An example of an HDL raising agent is nicotinic acid.

It is suggested that thiazolidinedione compounds exert their effects by binding to the peroxisome proliferator activated receptor (PPAR) family of receptors, controlling certain transcription elements having to do with the biological entities listed above. See Hulin et al., Current Pharm. Design (1996) 2, 85-102. Three sub-types of PPARs have been discovered and described: PPARα, PPARγ and PPARδ. PPARα is activated by a number of medium and long-chain fatty acids. It is involved in stimulating β–oxidation of fatty acids. PPARα is also activated by compounds known as fibric acid derivatives. These fibric acid derivatives, such as clofibrate, fenofibrate, bezafibrate, ciprofibrate, beclofibrate and etofibrate, as well as gemfibrozil reduce plasma triglycerides along with LDL cholesterol, and they are primarily used for the treatment of hypertriglyceridemia.

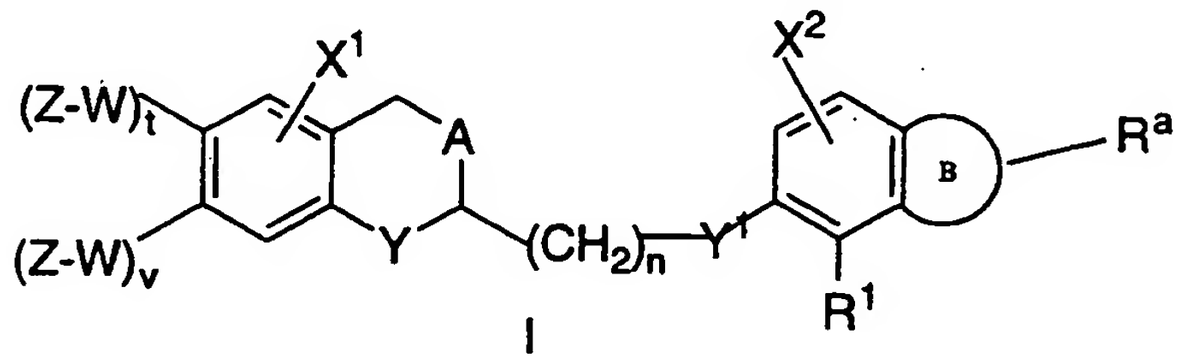
PPARγ receptor subtypes are involved in adipocyte differentiation. The DNA sequences for the PPARγ receptors are

described in Elbrecht, et al., BBRC *224*;431-437 (1996). Although peroxisome proliferators, including the fibrates and fatty acids, activate the transcriptional activity of PPARs, only prostaglandin J_2 derivatives have been identified as natural ligands of the PPARγ subtype, which also binds to thiazolidinedione antidiabetic agents with high affinity. The glitazones have been shown to bind to the PPARγ subtype.

The human nuclear receptor gene PPARδ (hPPARδ) has been cloned from a human osteosarcoma cell cDNA library and is fully described in A. Schmidt et al., *Molecular Endocrinology*, *6* :1634-1641 (1992), herein incorporated by reference. PPARδ is also referred as PPARβ and NUC1.

SUMMARY OF THE INVENTION

The present invention is directed to a compound represented by formula I or Ia:



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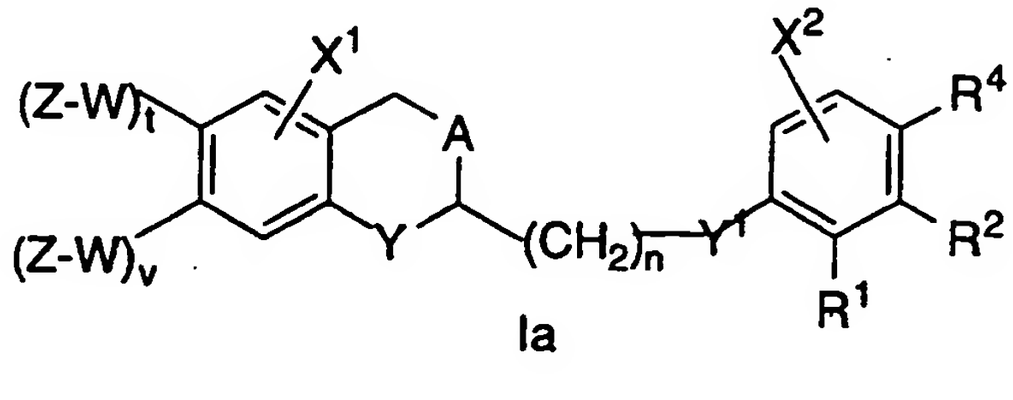


Ia

or a pharmaceutically acceptable salt thereof, wherein:

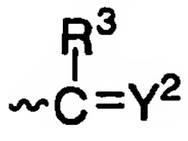
A is optionally a single or double bonded carbon or a single or double bond;

R^1 is selected from a group consisting of: H, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl and C_{3-10} cycloalkyl, said alkyl, alkenyl, alkynyl, and cycloalkyl optionally substituted with 1 to 3 groups of R^a;

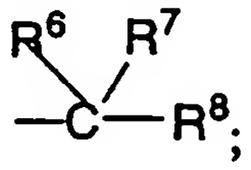
R^2 is selected from a group consisting of: H, C_{1-15} alkyl, C_{2-15} alkenyl, OR^3, CO_2alkyl, COalkyl, OH, $-OC(O)R^3$, C_{2-15} alkynyl, C_{5-10} aryl, C_{5-10} heteroaryl, said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R^a;

R^3 is selected from a group consisting of: H, NHR^1, NHacyl, C_{1-15} alkyl, C_{2-15} alkenyl, C_{1-15} alkoxy, CO_2alkyl, OH, C_{2-15} alkynyl, C_{5-10} aryl, C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R^a;

R^4 is selected from the group consisting of: R^2, $-D-R^5$ or



R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl optionally substituted with 1 to 3 groups of R^a;

W is $-CR^6R^7-$, or  ;

R^8 is selected from the group consisting of CR^6R^7, O, NR^6, and $S(O)_p$;

R^6 and R^7 are independently selected from the group consisting of H, C_{1-6} alkyl;

B is – a 5 or 6 membered heterocycle containing 0 to 2 double bonds, and 0 to 3 heteroatoms selected from the group consisting of O, S and N, the heteroatom being substituted at any position on the five or six membered heterocycle, the heterocycle being optionally unsubstituted or substituted with 1 to 3 groups of R^a;

D is selected from the group consisting of: O, S(O)p and NR^1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, halo, OR^3, C_{5-10} aryl, C_{5-10} aralkyl, C_{5-10} heteroaryl and C_{1-10} acyl, said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R^a;

R^a represents a member selected from the group consisting of: halo, aryl, heteroaryl, CF_3, OCF_3, -O-, CN, NO_2, R^3, OR^3; SR^3, $S(O)R^3$, SO_2R^3, NR^3R^3, NR^3COR^3, $NR^3CO_2R^3$, $NR^3CON(R^3)_2$, $NR^3SO_2R^3$, COR^3, CO_2R^3, $CON(R^3)_2$, $SO_2N(R^3)_2$, $OCON(R^3)_2$ said aryl and heteroaryl optionally substituted with 1 to 3 groups of halo or C1-6 alkyl;

Y is selected from the group consisting of: $S(O)_p$, $-CH_2-$, CO, NR^1, O, SO_2NH, $NHSO_2$;

Y^2 is selected from the group consisting of: O, $N(C_{1-15})$ alkyl, $N(CO_2)$alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 then n is 2;

Y^1 is selected from the group consisting of: O, NH, $S(O)_p$ and C;

Z is selected from the group consisting of: CO_2R^3, $R^3CO_2R^3$, $CONHSO_2Me$, $CONH_2$ and 5-(1H-tetrazole); or

$(Z\text{-}W)_t$ or $(Z\text{-}W)_v$ together with X^1 can form a 5 or 6 membered ring, said ring being a carbocycle, aryl or heteroaryl and optionally substituted with 1 to 3 groups of R^a; in the cas where $(Z\text{-}W)_t$ is used v is 0 or 1; in the case where $(Z\text{-}W)_v$ is used t is 0 or 1;

t and v are independently 0 or 1 such that t + v = 1;

n is 2-4 and

p is 0-2.

Also included in the invention is a pharmaceutical composition which is comprised of a compound of formula I or Ia in combination with a pharmaceutically acceptable carrier.

Also included in the invention is a pharmaceutical composition which is comprised of a compound of formula I or Ia in combination with one or more known sulfonylureas, biguanides, α-glucosidase inhibitors, other insulin secretogogues or insulin.

Also included in the invention is a method for raising high density lipoprotein (HDL) plasma levels in a mammal in need of such treatment comprising administering an effective amount of a compound of formula I or Ia.

Also included in the invention is a method for preventing, halting, slowing or otherwise treating the progression of atherosclerotic cardiovascular diseases and related conditions and disease events in a mammal in need of such treatment comprising administering an effective amount of a compound of formula I or Ia.

Also included in the invention is a method for preventing, halting or slowing the progression of atherosclerotic cardiovascular diseases and related conditions and disease events in a mammal in need of such treatment comprising administering an effective amount of a compound of formula I or Ia in combination with one or more active agents such as antihyperlipidemic agents, HMG-CoA synthase inhibitors, squalene epoxidase inhibitors and the like.

Also included in the invention is a method of treating or controlling diabetes and related diseases such as diabetic retinopathy, diabetic nephropathy and the like, which comprises administering to a mammalian diabetic patient an effective amount of a compound of formula I or Ia.

Also included in the invention is a method of treating or controlling diabetes and related diseases such as diabetic

retinopathy; diabetic nephropathy and the like, which comprises administering a compound of formula I or Ia in combination with one or more known sulfonylureas, biguanides, α-glucosidase inhibitors, other insulin secretogogues or insulin.

Also included in the present invention is a method of treating pancreatitis in a mammalian patient in need of such treatment, which is comprised of administering to said patient an amount of a compound of formula I or Ia which is effective for treating pancreatitis.

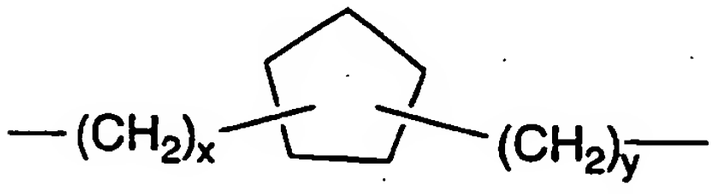
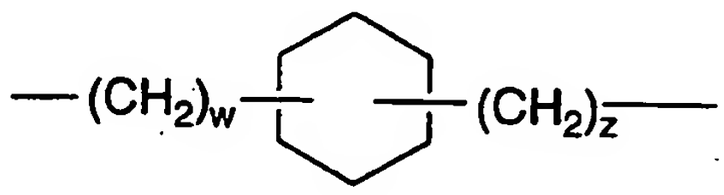
DESCRIPTION OF THE INVENTION

The invention is described herein in detail using the terms defined below unless otherwise specified.

The term "alkyl" and the alkyl portion of "acyl" refer to a monovalent alkane (hydrocarbon) derived radical containing from 1 to 15 carbon atoms unless otherwise defined. It may be straight, branched or cyclic. Preferred straight or branched alkyl groups include methyl, ethyl, propyl, isopropyl, butyl and t-butyl. Preferred cycloalkyl groups include cyclopentyl and cyclohexyl.

The carbon chain of "acyl" also includes alkenyl and alkynyl groups as described below, with the double or triple bonds being located in appropriate positions within the chain.

Alkyl also includes a straight or branched alkyl group which contains or is interrupted by a cycloalkylene portion. Examples include the following:


and


wherein: x and y = from 0-10; and w and z = from 0-9.

The alkylene and monovalent alkyl portion(s) of the alkyl group can be attached at any available point of attachment to the cycloalkylene portion.

When substituted alkyl is present, this refers to a straight, branched or cyclic alkyl group as defined above, substituted with 1-3 groups as defined with respect to each variable.

The term "alkenyl" refers to a hydrocarbon radical straight, branched or cyclic containing from 2 to 15 carbon atoms and at least one carbon to carbon double bond. Preferably one carbon to carbon double bond is present, and up to four non-aromatic (non-resonating) carbon-carbon double bonds may be present. Preferred alkenyl groups include ethenyl, propenyl, butenyl and cyclohexenyl. As described above with respect to alkyl, the straight, branched or cyclic portion of the alkenyl group may contain double bonds and may be substituted when a substituted alkenyl group is provided.

The term "alkynyl" refers to a hydrocarbon radical straight, branched or cyclic, containing from 2 to 15 carbon atoms and at least one carbon to carbon triple bond. Up to three carbon-carbon triple bonds may be present. Preferred alkynyl groups include ethynyl, propynyl and butynyl. As described above with respect to alkyl, the straight, branched or cyclic portion of the alkynyl group may contain triple bonds and may be substituted when a substituted alkynyl group is provided.

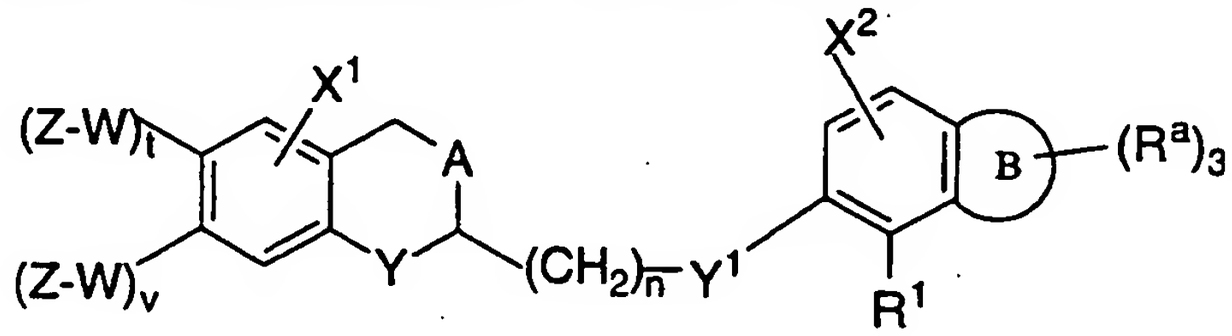
The term "alkoxy" refers to those groups of the designated carbon length in either a straight or branched configuration attached through an oxygen linkage and if two or more carbon atoms in length, they may include a double or a triple bond. Exemplary of such alkoxy groups are methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, tertiary butoxy, pentoxy, isopentoxy, hexoxy, isohexoxy, allyloxy, propargyloxy, and the like.

The term halo as used herein, represents fluoro, chloro, bromo or iodo.

Aryl refers to aromatic rings e.g., phenyl, substituted phenyl and like groups as well as rings which are fused, e.g., naphthyl and the like. Aryl thus contains at least one ring having at least 5 atoms, with up to two such rings being present, containing up to 10 atoms therein, with alternating (resonating) double bonds between adjacent carbon atoms. The preferred aryl groups are phenyl and naphthyl. Aryl groups may likewise be substituted with 0-3 groups selected from R^a. The preferred aryl groups are phenyl and naphthyl. Aryl groups may likewise be substituted as defined below. Preferred substituted aryls include phenyl and naphthyl substituted with zero or three groups of R^a.

Heteroaryl is a group containing from 5 to 10 atoms, 1-4 of which are heteroatoms, 0-4 of which heteroatoms are N and 0-1 of which are O or S, said heteroaryl group being unsubstituted or substituted with 0-3 R^a groups; examples of heteroaryls are pyridyl, quinolyl, purinyl, imidazolyl, imidazopyridyl and pyrimidinyl

A subset of compounds of the invention is included herein and described in connection with formula I or Ia:



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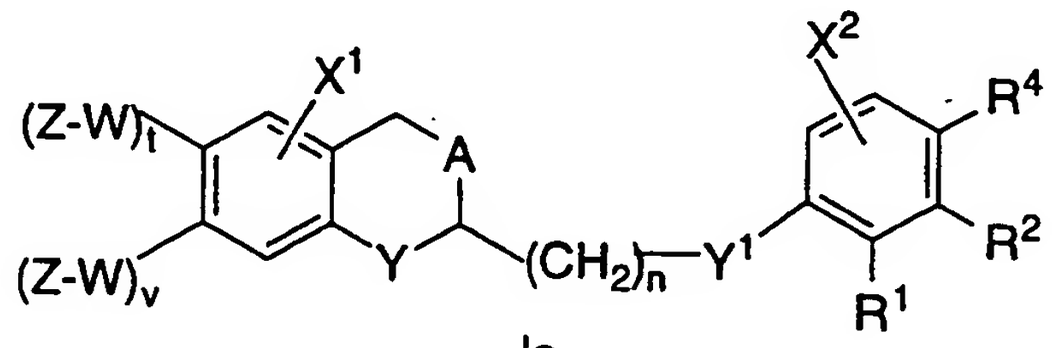


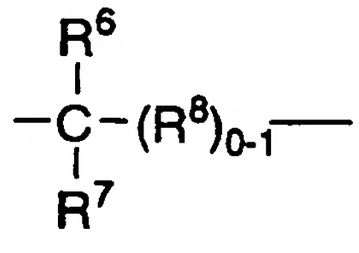
Ia

as well as pharmaceutically acceptable salts thereof, wherein:

A represents a single or double bonded carbon, or a direct single or double bond;

Y represents a member selected from the group consisting of: $-S(O)_p-$ wherein p is 0, 1 or 2, , $-CH_2-$, -C(O)- , $-NR^1-$, -O-, $-SO_2NH-$ and $-NHSO_2-$;

one of t and v is zero and the other is 1;

W is  , and

Z is selected from the group consisting of: $CO_2R^{3'}$, $CONHSO_2C_{1-6}$ alkyl, $CONH_2$ and 5-(1H-tetrazolyl); or in the alternative,

one of $(Z\text{-}W)_t$ and $(Z\text{-}W)_v$ is taken in combination with X^1 to represent a 5 or 6 membered fused ring, said ring being a carbocycle, aryl or heteroaryl ring, and being optionally substituted with 1 to 3 R^a groups;

when $(Z\text{-}W)_t$ is taken in combination with X^1, v is 0 or 1, and when $(Z\text{-}W)_v$ is taken in combination with X^1, t is 0 or 1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{2\text{-}15}$ alkynyl, halo, $C_{5\text{-}10}$ aryl, $C_{5\text{-}10}$ heteroaryl, $C_{1\text{-}10}$ acyl, $C_{1\text{-}5}$ alkoxy, $C_{5\text{-}10}$ aryloxy, $C_{2\text{-}15}$ alkenyloxy, $C_{2\text{-}15}$ alkynyloxy, heteroaryloxy, $C_{1\text{-}10}$ acyloxy

said alkyl, alkenyl, alkynyl, aryl, acyl and heteroaryl, and the alkyl, alkenyl, alkynyl, aryl acy and heteroaryl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

n is 2, 3 or 4;

Y^1 represents O, NH, CH_2 or $S(O)_p$ wherein p is as defined above;

B represents a 5 or 6 membered fused ring containing 0 to 2 double bonds, and optionally containing 1 to 3 heteroatoms selected from the group consisting of O, S and N, said ring being optionally substituted with 1 to 3 R^a groups;

R^1 is selected from a group consisting of: H, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl and $C_{2\text{-}15}$ alkynyl, said alkyl, alkenyl and alkynyl being optionally substituted with 1 to 3 R^a groups;

R^2 is selected from a group consisting of: H, OH, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{2\text{-}15}$ alkynyl, $C_{5\text{-}10}$ aryl, $C_{5\text{-}10}$ heteroaryl, $-C(O)C_{1\text{-}15}$ alkyl, $CO_2C_{1\text{-}6}$ alkyl, $-OC(O)R^{3'}$, $C_{1\text{-}6}$ alkoxy, $C_{5\text{-}10}$ aryloxy, $C_{2\text{-}15}$ alkenyloxy, $C_{2\text{-}15}$ alkynyloxy, heteroaryloxy and $C_{1\text{-}10}$ acyloxy,

said alkyl, alkenyl, alkynyl, aryl and heteroaryl, and the alkyl, aryl, alkenyl, alkynyl heteroaryl and acyl portions of alkoxy,

aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

R^3 is selected from a group consisting of: H, OH, NHR^1, NHacyl, C_{1-15} alkyl, C_{2-15} alkenyl, C_{1-15} alkoxy, CO_2alkyl, C_{2-15} alkynyl, C_{5-10} aryl, and C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 R^a groups;

each R^a independently represents a member selected from the group consisting of: $R^{3'}$, halo, CF_3, OCF_3, CN, NO_2, , $OR^{3'}$, $S(O)_p$-$R^{3'}$; $N(R^{3'})_2$, $NR^{3'}COR^{3'}$, $NR^{3'}CO_2R^{3'}$, $NR^{3'}CON(R^{3'})_2$, $NR^{3'}SO_2R^{3'}$, $C(O)R^{3'}$, $CO_2R^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, $OCON(R^{3'})_2$, and when $R^{3'}$ is present and represents alkyl, alkenyl, alkynyl, aryl or heteroaryl, said alkyl, alkenyl, alkynyl, aryl or heteroaryl group is optionally substituted with 1 to 3 halo, hydroxy, C_{1-3} alkoxy, carboxy or amino groups, and

when at least two R^a groups are present, they may also be taken in combination with any intervening atoms to represent a 4-6 membered ring, said ring containing 0-3 heteroatoms selected from O, $S(O)_p$ and N, and said ring being optionally interrupted by 1-2 -C(O)- groups, and optionally substituted with 1-3 halo, hydroxy, C_{1-6} alkyl or amino groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl;

R^4 represents R^2, -D-R^5 or  ;

D is selected from O, S(O)p ,NR^1 and CR^6R^7;

R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl being optionally substituted with 1 to 3 R^a groups;

Y^2 is selected from the group consisting of: O, $N(C_{1-15})$ alkyl, $N(CO_2)$alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 then n is 2;

R^8 is optional and is selected from the group consisting of CR^6R^7, O, NR^6 and $S(O)_p$,

and R^6 and R^7 are independently selected from H and C_{1-6} alkyl.

One embodiment of the invention which is particular interest is realized when Y is O and all other variables are as described above.

Another embodiment of the invention is realized when Y is $S(O)_p$, p is 0-2 and all other variables are described as above.

Still another embodiment of the invention is realized when Y is $-CH_2-$ and all other variables are described as above.

Yet another embodiment of the invention is realized when Y is CO and all other variables are described as above.

A further embodiment of the invention is realized when Y is NH and all other variables are described as above.

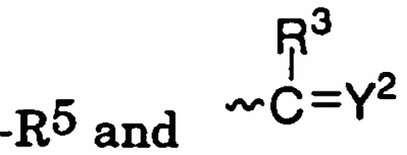
Another embodiment of the invention is realized when Y is $NHSO_2$ or SO_2NH and all other variables are described as above.

Another embodiment of the invention is realized when $(Z\text{-}W)_t$ or $(Z\text{-}W)_v$ together with X^1 form a 5 or 6 membered ring, said ring being a carbocycle, aryl or heteroaryl and optionally substituted with 1 to 3 R^a groups. In the case where $(Z\text{-}W)_t$ is used, v is 0 or 1; in the case where $(Z\text{-}W)_v$ is used, t is 0 or 1; and all other variables are described as above.

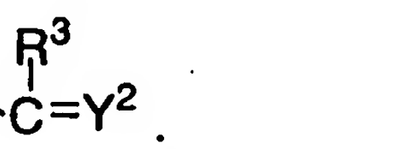
Another embodiment of the novel compounds of the instant invention is realized when A is a single or double bonded carbon and all other variables are described as above.

Still another embodiment of the novel compounds of the instant invention is realized when A is a single or double bond and all other variables are described as above.

Still another embodiment of the invention is realized when B is a 5 or 6 membered heterocycle containing 0 to 2 double bonds, and 1 to 3 heteroatoms selected from the group consisting of O, S and N, the heteroatom being present at any position in the five or six membered ring, the heterocycle being unsubstituted or substituted with 1 to 3 R^a groups, and all other variables are described as above.

Still another embodiment of the novel compounds of the instant invention is realized when R^4 is selected from the group consisting of: R^2, -D-R^5 and  and all other variables are described as above. Preferably R^4 represents R^2 or -D-R^5.

A preferred embodiment of the invention is realized when:
R^1 is H or $C_{1\text{-}15}$ alkyl;
X^1 and X^2 are independently H or halo;
B is a 5 or 6 membered heterocycle containing 0 to 2 double bonds, and 1 to 3 heteroatoms selected from the group consisting of O, S and N, the heteroatom being at any allowable position in the five or six membered heterocycle, the heterocycle being unsubstituted or substituted with 1 to 3 R^a groups;
Y is O, NH or S;
Y^1 is O;
W is -CR^6R^7-;
R^a is a member selected from the group consisting of: halo, aryl, heteroaryl, CF_3, OCF_3, -O-, CN, NO_2, $R^{3'}$, $OR^{3'}$; $SR^{3'}$, $S(O)R^{3'}$, $SO_2R^{3'}$, $NR^{3'}COR^{3'}$, $COR^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, said aryl and heteroaryl optionally substituted with 1 to 3 halo or C1-6 alkyl groups; and
Z is $CO_2R^{3'}$, $CONHSO_2Me$, $CONH_2$ or 5-(1H-tetrazolyl). All other variables are as originally defined.

Another preferred embodiment of the invention is realized when:
R^1 is H or $C_{1\text{-}15}$ alkyl;
-R^4 is R^2, -D-R^5 or  ;
X^1 and X^2 are independently H or halo;
Y is O, NH or S;
Y^1 is O;
W is -CR^6R^7-;

R^a is a member selected from the group consisting of: halo, aryl, heteroaryl, CF_3, OCF_3, -O-, CN, NO_2, $R^{3'}$, $OR^{3'}$; $SR^{3'}$, $S(O)R^{3'}$, $SO_2R^{3'}$, $NR^{3'}COR^{3'}$, $COR^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, wherein $R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl, said aryl and heteroaryl optionally substituted with 1 to 3 groups of halo or C_{1-6} alkyl; and

Z is $CO_2R^{3'}$, $CONHSO_2Me$, $CONH_2$ or 5-(1H-tetrazolyl).

Still another preferred embodiment of the invention is realized when:

R^1 is C_{1-15} alkyl;

R^4 is $-D-R^5$ or $\sim C(R^3)=Y^2$;

X^2 is H, or halo;

Y is O, NH or S;

Y^1 is O;

R^a is a member selected from the group consisting of: halo, aryl, heteroaryl, CF_3, OCF_3, -O-, CN, NO_2, $R^{3'}$, $OR^{3'}$; $SR^{3'}$, $S(O)R^{3'}$, $SO_2R^{3'}$, $NR^{3'}COR^{3'}$, $COR^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, said aryl and heteroaryl optionally substituted with 1 to 3 halo or C_{1-6} alkyl groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl, said aryl and heteroaryl optionally substituted with 1 to 3 halo or C_{1-6} alkyl groups;

$(Z\text{-}W)_t$ or $(Z\text{-}W)_v$ together with X^1 forms a 5 or 6 membered ring, said ring being a carbocycle, aryl or heteroaryl and optionally substitut d with 1 to 3 R^a groups; in the case where $(Z\text{-}W)_t$ is used v is 0 or 1; in the

case where $(Z\text{-}W)_v$ is used t is 0 or 1; and all other variables are described as above.

Examples of compounds of the invention include the following:

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-indole-5-acetic acid;

2-(2-(3-(2,2-Dimethylpropyl)-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-indole-5-(2,2-dimethyl)acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-indole-5-propan-3-oic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-indole-5-propan-3-oic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-indole-5-oxyacetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-indole-5-oxyacetic acid;

N-[2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-indol-5-yl]glycine;

N-[2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-indol-5-yl]glycine;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-indole-6-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-indole-6-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-4-chloroindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-4-chloroindole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-quinolin-6-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-quinolin-6-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-quinolin-7-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-quinolin-7-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-quinazolin-6-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-quinazolin-6-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-quinazolin-7-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-quinazolin-7-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-3-methylindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-3-methylindole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-3-butylindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-3-butylindole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-7-propylindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-7-propylindole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-N-methylindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-N-methylindole-5-acetic acid;

2-(3-(3-Phenyl-7-propylbenzofuran-6-yloxy)propyl)indole-5-acetic acid;

2-(3-(3-Neopentyl-7-propylbenzofuran-6-yloxy)propyl)indole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)propyl)indole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)propyl)indole-5-acetic acid;

2-(2-(3-Phenyl-7-(cyclopropylmethyl)benzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Neopentyl-7-(cyclopropylmethyl)benzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(1-Phenyl-4-propylindol-5-yloxy)ethyl)indole-5-acetic acid;

2-(2-(1-Phenyl-4-propylindol-5-yloxy)ethyl)benzofuran-5-acetic acid;

2-(2-(1-Phenyl-4-propylindol-5-yloxy)ethyl)indole-5-oxyacetic acid;

2-(2-(1-Phenyl-4-propylindol-5-yloxy)ethyl)indole-5-propan-3-oic acid;

2-(2-(4-Phenoxy-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-(4-Tolyloxy)-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-Valeryl-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-Benzoyl-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-(N-Hydroxyimino)valeryl-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-(N-Hydroxyimino)benzoyl-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(3-(3-Fluorophenyl)-7-propylbenzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-(Phen-2-ethyl)-7-propylbenzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-(4-t-Butylphenyl)-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-(2,2-Dimethyl-2-phenylethyl)-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid sodium salt;

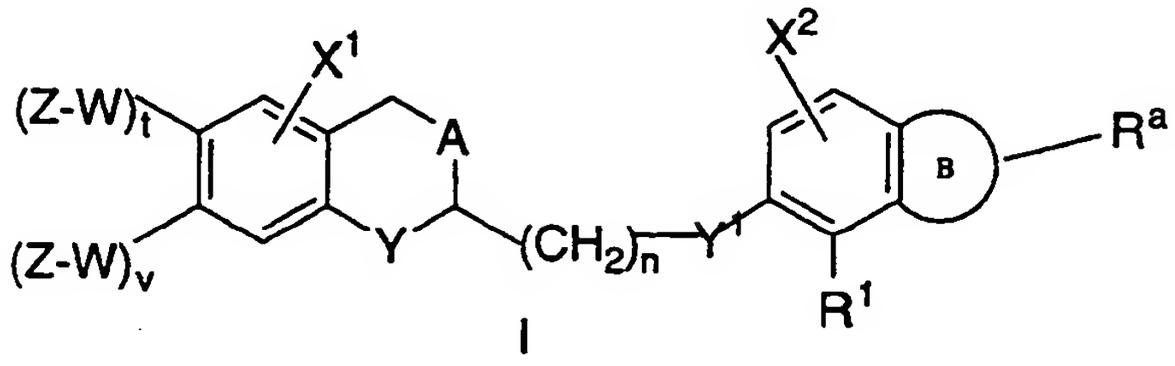
2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid methyl ester;

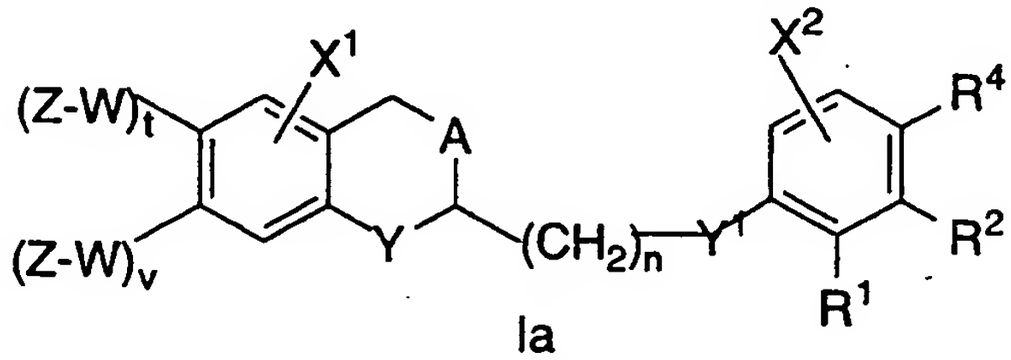
2-(2-(3-(2-Phenyl)ethyl-7-(n-propyl)benz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

WHAT IS CLAIMED IS:

1. A compound having the formula I or Ia:



I



Ia

or a pharmaceutically acceptable salt thereof, wherein:

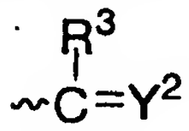
A is optionally a single or double bonded carbon or a single or double bond;

R^1 is selected from a group consisting of: H, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl and C_{3-10} cycloalkyl, said alkyl, alkenyl, alkynyl, and cycloalkyl optionally substituted with 1 to 3 groups of R^a;

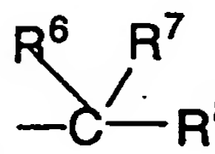
R^2 is selected from a group consisting of: H, C_{1-15} alkyl, C_{2-15} alkenyl, OR^3, CO_2alkyl, COalkyl, OH, $-OC(O)R^3$, C_{2-15} alkynyl, C_{5-10} aryl, C_{5-10} heteroaryl, said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R^a;

R^3 is selected from a group consisting of: H, NHR^1, NHacyl, C_{1-15} alkyl, C_{2-15} alkenyl, C_{1-15} alkoxy, CO_2alkyl, OH, C_{2-15} alkynyl, C_{5-10} aryl, C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R^a;

R^4 is selected from the group consisting of: R^2, -D-R^5 or



R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl optionally substituted with 1 to 3 groups of R^a;

W is -CR^6R^7-, or  ;

R^8 is selected from the group consisting of CR^6R^7, O, NR^6, and $S(O)_p$;

R^6 and R^7 are independently selected from the group consisting of H, C_{1-6} alkyl;

B is a 5 or 6 membered heterocycle containing 0 to 2 double bonds, and 0 to 3 heteroatoms selected from the group consisting of O, S and N, the heteroatom being substituted at any position on the five or six membered heterocycle, the heterocycle being optionally unsubstituted or substituted with 1 to 3 groups of R^a;

D is selected from the group consisting of: O, S(O)p and NR^1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, halo, OR^3, C_{5-10} aryl, C_{5-10} aralkyl, C_{5-10} heteroaryl and C_{1-10} acyl, said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R^a;

R^a represents a member selected from the group consisting of: halo, aryl, heteroaryl, CF_3, OCF_3, -O-, CN, NO_2, R^3, OR^3; SR^3, $S(O)R^3$, SO_2R^3, NR^3R^3, NR^3COR^3, $NR^3CO_2R^3$,

$NR^3CON(R^3)_2$, $NR^3SO_2R^3$, COR^3, CO_2R^3, $CON(R^3)_2$, $SO_2N(R^3)_2$, $OCON(R^3)_2$ said aryl and heteroaryl optionally substituted with 1 to 3 groups of halo or C1-6 alkyl;

Y is selected from the group consisting of: $S(O)_p$, $-CH_2-$, CO, NR^1, O, SO_2NH, $NHSO_2$;

Y^2 is selected from the group consisting of: O, $N(C_{1-15})$ alkyl, $N(CO_2)$alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 then n is 2;

Y^1 is selected from the group consisting of: O, NH, $S(O)_p$ and C;

Z is selected from the group consisting of: CO_2R^3, $R^3CO_2R^3$, $CONHSO_2Me$, $CONH_2$ and 5-(1H-tetrazole);

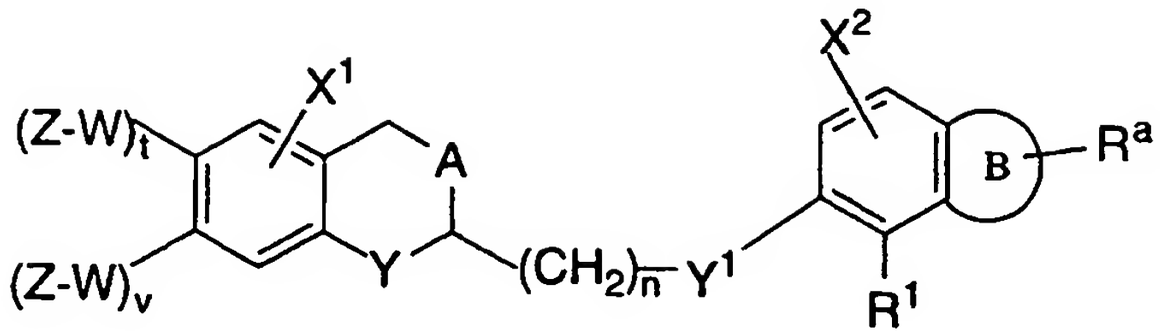
$(Z-W)_t$ or $(Z-W)_v$ together with X^1 can form a 5 or 6 membered ring, said ring being a carbocycle, aryl or heteroaryl and optionally substituted with 1 to 3 groups of R^a; in the case where $(Z-W)_t$ is used v is 0 or 1; in the case where $(Z-W)_v$ is used t is 0 or 1;

t and v are independently 0 or 1 such that t + v = 1;

n is 2-4 and

p is 0-2.

2. A compound represented by formula I or Ia:



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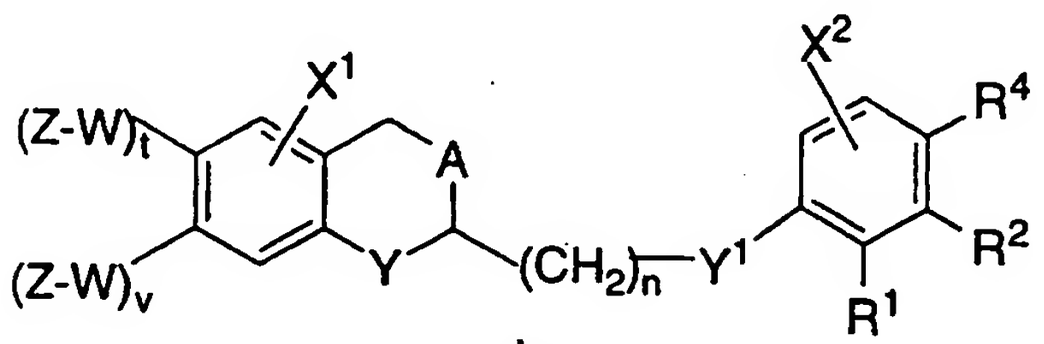


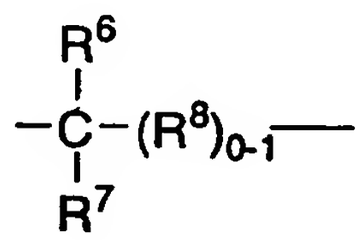
Ia

or a pharmaceutically acceptable salt thereof, wherein:

A represents a single or double bonded carbon, or a direct single or double bond;

Y represents a member selected from the group consisting of: $-S(O)_p-$ wherein p is 0, 1 or 2, , $-CH_2-$, -C(O)- , $-NR^1-$, -O-, $-SO_2NH-$ and $-NHSO_2-$;

one of t and v is zero and the other is 1;



W is , and

Z is selected from the group consisting of: $CO_2R^{3'}$, $CONHSO_2C_{1-6}$ alkyl, $CONH_2$ and 5-(1H-tetrazolyl); or in the alternative,

one of $(Z\text{-}W)_t$ and $(Z\text{-}W)_v$ is taken in combination with X^1 to represent a 5 or 6 membered fused ring, said ring being a carbocycle, aryl or heteroaryl ring, and being optionally substituted with 1 to 3 R^a groups;

when $(Z\text{-}W)_t$ is taken in combination with X^1, v is 0 or 1, and when $(Z\text{-}W)_v$ is taken in combination with X^1, t is 0 or 1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{2\text{-}15}$ alkynyl, halo, $C_{5\text{-}10}$ aryl, $C_{5\text{-}10}$ heteroaryl, $C_{1\text{-}10}$ acyl, $C_{1\text{-}5}$ alkoxy, $C_{5\text{-}10}$ aryloxy, $C_{2\text{-}15}$ alkenyloxy, $C_{2\text{-}15}$ alkynyloxy, heteroaryloxy, $C_{1\text{-}10}$ acyloxy

said alkyl, alkenyl, alkynyl, aryl, acyl and heteroaryl, and the alkyl, alkenyl, alkynyl, aryl acy and heteroaryl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

n is 2, 3 or 4;

Y^1 represents O, NH, CH_2 or $S(O)_p$ wherein p is as defined above;

B represents a 5 or 6 membered fused ring containing 0 to 2 double bonds, and optionally containing 1 to 3 heteroatoms selected from the group consisting of O, S and N, said ring being optionally substituted with 1 to 3 R^a groups;

R^1 is selected from a group consisting of: H, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl and $C_{2\text{-}15}$ alkynyl, said alkyl, alkenyl and alkynyl being optionally substituted with 1 to 3 R^a groups;

R^2 is selected from a group consisting of: H, OH, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{2\text{-}15}$ alkynyl, $C_{5\text{-}10}$ aryl, $C_{5\text{-}10}$ heteroaryl, $-C(O)C_{1\text{-}15}$ alkyl, $CO_2C_{1\text{-}6}$ alkyl, $-OC(O)R^{3'}$, $C_{1\text{-}6}$ alkoxy, $C_{5\text{-}10}$ aryloxy, $C_{2\text{-}15}$ alkenyloxy, $C_{2\text{-}15}$ alkynyloxy, heteroaryloxy and $C_{1\text{-}10}$ acyloxy,

said alkyl, alkenyl, alkynyl, aryl and heteroaryl, and the alkyl, aryl, alkenyl, alkynyl heteroaryl and acyl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

R^3 is selected from a group consisting of: H, OH, NHR^1, NHacyl, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{1\text{-}15}$ alkoxy, CO_2alkyl, $C_{2\text{-}15}$

alkynyl, C_{5-10} aryl, and C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 R^a groups;

each R^a independently represents a member selected from the group consisting of: $R^{3'}$, halo, CF_3, OCF_3, CN, NO_2, , $OR^{3'}$, $S(O)_p$-$R^{3'}$; $N(R^{3'})_2$, $NR^{3'}COR^{3'}$, $NR^{3'}CO_2R^{3'}$, $NR^{3'}CON(R^{3'})_2$, $NR^{3'}SO_2R^{3'}$, $C(O)R^{3'}$, $CO_2R^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, $OCON(R^{3'})_2$, and when $R^{3'}$ is present and represents alkyl, alkenyl, alkynyl, aryl or heteroaryl, said alkyl, alkenyl, alkynyl, aryl or heteroaryl group is optionally substituted with 1 to 3 halo, hydroxy, C_{1-3} alkoxy, carboxy or amino groups, and when at least two R^a groups are present, they may also be taken in combination with any intervening atoms to represent a 4-6 membered ring, said ring containing 0-3 heteroatoms selected from O, $S(O)_p$ and N, and said ring being optionally interrupted by 1-2 -C(O)- groups, and optionally substituted with 1-3 halo, hydroxy, C_{1-6} alkyl or amino groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl;

R^4 represents R^2, -D-R^5 or ;

D is selected from O, S(O)p ,NR^1 and CR^6R^7;

R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl being optionally substituted with 1 to 3 R^a groups;

Y^2 is selected from the group consisting of: O, $N(C_{1-15})$ alkyl, $N(CO_2)$alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 then n is 2;

R^8 is optional and is selected from the group consisting of CR^6R^7, O, NR^6 and $S(O)_p$,

and R^6 and R^7 are independently selected from H and C_{1-6} alkyl.

3. A compound of Claim 1 where X^1 and X^2 are independently H or halo.

4. A compound of Claim 1 where Y is O.

5. A compound of Claim 1 where Y is $S(O)_p$, wherein p is 0-2.

6. A compound of Claim 1 where Y is $-CH_2-$.

7. A compound of Claim 1 where Y is -CO-.

8. A compound of Claim 1 where Y is -NH-.

9. A compound of Claim 1 where Y is $NHSO_2$ or SO_2NH.

10. A compound of Claim 1 where A is a single or double bonded carbon .

11. A compound of Claim 1 where A is a single or double bond.

12. A compound of Claim 1 where B is a 5 or 6 membered heterocycle containing 0 to 2 double bonds, and 0 to 3 heteroatoms selected from the group consisting of O, S and N, the heteroatom being substituted at any position on the five or six membered heterocycle, the heterocycle being optionally unsubstituted or substituted with 1 to 3 groups of R^a.

13. A compound of Claim 1 where R^4 is selected from the group consisting of: R^2, $-D-R^5$ or $\sim C(R^3)=Y^2$

14. A compound of Claim 1 wherein:
$(Z\text{-}W)_t$ or $(Z\text{-}W)_v$ together with X^1 forms a 5 or 6 membered ring, said ring being a carbocycle, aryl or heteroaryl and optionally substituted with 1 to 3 groups of R^a; in the case where $(Z\text{-}W)_t$ is used v is 0 or 1; in the case where $(Z\text{-}W)_v$ is used t is 0 or 1; and all other variables are described as above.

15. A compound of Claim 1 wherein

R^1 is	H or $C_{1\text{-}15}$ alkyl;
X^1 and X^2 are	independently H, or halo;
B is	a 5 or 6 membered heterocycle containing 0 to 2 double bonds, and 0 to 3 heteroatoms selected from the group consisting of O, S and N, the heteroatom being substituted at any position on the five or six membered heterocycle, the heterocycle being optionally unsubstituted or substituted with 1 to 3 R^a groups;
Y is	O, NH or S;
Y^1 is	O;
W is	$-CR^6R^7-$;
R^a is	a member selected from the group consisting of: halo, aryl, heteroaryl, CF_3, OCF_3, -O-, CN, NO_2, $R^{3'}$, $OR^{3'}$; $SR^{3'}$, $S(O)R^{3'}$, $SO_2R^{3'}$, $NR^{3'}COR^{3'}$, $COR^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, said aryl and heteroaryl optionally substituted with 1 to 3 halo or C1-6 alkyl groups;
$R^{3'}$	represents H, $C_{1\text{-}6}$ alkyl, $C_{2\text{-}6}$ alkenyl, $C_{2\text{-}6}$ alkynyl, aryl or heteroaryl; and
Z is	$CO_2R^{3'}$, $CONHSO_2Me$, $CONH_2$ or 5-(1H-tetrazole).

16. A compound of Claim 1 wherein:

R^1 is H or C_{1-15} alkyl;

X^1 and X^2 are independently H, or halo;

R^4 is selected from the group consisting of: R^2, -D-R^5 or ;

Y is O, NH or S;

Y^1 is O;

W is -CR^6R^7-;

R^a is a member selected from the group consisting of: halo, aryl, heteroaryl, CF_3, OCF_3, -O-, CN, NO_2, $R^{3'}$, $OR^{3'}$; $SR^{3'}$, $S(O)R^{3'}$, $SO_2R^{3'}$, $NR^{3'}COR^{3'}$, $COR^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, said aryl and heteroaryl optionally substituted with 1 to 3 halo or C1-6 alkyl groups ;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl; and

Z is $CO_2R^{3'}$, $CONHSO_2Me$, $CONH_2$ or 5-(1H-tetrazole).

17. A compound of Claim 1 wherein:

R^1 is C_{1-15} alkyl;

R^4 is -D-R^5 or  ;

X^2 is H, or halo;

Y is O, NH or S;

Y^1 is O;

R^a is a member selected from the group consisting of: halo, aryl, heteroaryl, CF_3, OCF_3, -O-, CN, NO_2, $R^{3'}$, $OR^{3'}$; $SR^{3'}$, $S(O)R^{3'}$, $SO_2R^{3'}$, $NR^{3'}COR^{3'}$, $COR^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, said aryl and heteroaryl optionally substituted with 1 to 3 halo or C1-6 alkyl groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl; and

$(Z\text{-}W)_t$ or $(Z\text{-}W)_v$ together with X^1 forms a 5 or 6 membered ring, said ring being a carbocycle, aryl or heteroaryl and optionally substituted with 1 to 3 groups of R^a; in the case where $(Z\text{-}W)_t$ is used v is 0 or 1; in the case where $(Z\text{-}W)_v$ is used t is 0 or 1; and all other variables are described as above.

18. A compound of Claim 1 selected from the group consisting of:

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-indole-5-acetic acid;

2-(2-(3-(2,2-Dimethylpropyl)-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)indole-5-(2,2-dimethyl)acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-propan-3-oic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-propan-3-oic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)indole-5-oxyacetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)indole-5-oxyacetic acid;

N-[2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indol-5-yl]glycine;

N-[2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indol-5-yl]glycine;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)indole-6-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-indole-6-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-4-chloroindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-4-chloroindole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-quinolin-6-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-quinolin-6-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-quinolin-7-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-quinolin-7-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)quinazolin-6-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)quinazolin-6-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)quinazolin-7-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)quinazolin-7-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-3-methylindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-3-methylindole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-3-butylindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-3-butylindole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-7-propylindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)-7-propylindole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-N-methylindole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-N-methylindole-5-acetic acid;

2-(3-(3-Phenyl-7-propylbenzofuran-6-yloxy)propyl)indole-5-acetic acid;

2-(3-(3-Neopentyl-7-propylbenzofuran-6-yloxy)propyl)indole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)propyl)indole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)propyl)indole-5-acetic acid;

2-(2-(3-Phenyl-7-(cyclopropylmethyl)benzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Neopentyl-7-(cyclopropylmethyl)benzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(1-Phenyl-4-propylindol-5-yloxy)ethyl)indole-5-acetic acid;

2-(2-(1-Phenyl-4-propylindol-5-yloxy)ethyl)benzofuran-5-acetic acid;

2-(2-(1-Phenyl-4-propylindol-5-yloxy)ethyl)indole-5-oxyacetic acid;

2-(2-(1-Phenyl-4-propylindol-5-yloxy)ethyl)indole-5-propan-3-oic acid;

2-(2-(4-Phenoxy-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-(4-Tolyloxy)-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-Valeryl-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-Benzoyl-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-(N-Hydroxyimino)valeryl-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-(N-Hydroxyimino)benzoyl-3-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(3-(3-Fluorophenyl)-7-propylbenzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-(Phen-2-ethyl)-7-propylbenzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-(4-t-Butylphenyl)-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-(2,2-Dimethyl-2-phenylethyl)-7-propylbenzisoxazol-6-yloxy)ethyl)-indole-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid methyl ester;

2-(2-(3-(2-Phenyl)ethyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)benzofuran-5-acetic acid;

2-(2-(3-(2,2-Dimethylpropyl)-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)benzofuran-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)benzofuran -5-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-benzofuran-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl-4,5,6,7-tetrahydronaphtho[2,1-b]furan-7-carboxylic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-4,5,6,7-tetrahydronaphtho[2,1-b]furan-7-carboxylic acid; and

2-(2-(3-(2,2-Dimethylpropyl)-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-4,5,6,7-tetrahydronaphtho[2,1-b]furan-7-carboxylic acid

or a salt or hydrate thereof.

19. A compound in accordance with Claim 18 selected from the group consisting of:

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)benzothiophen-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenzofuran-6-yloxy)ethyl)benzofuran-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)benzofuran-5-acetic acid;

2-(2-(3-Neopentyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)benzothiophen-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid methyl ester;

2-(2-(3-(2-Phenyl)ethyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)benzofuran-5-acetic acid;

2-(2-(3-(2,2-Dimethylpropyl)-7-(n-propyl)benz[4,5]isoxazol-6-yloxy)ethyl)benzofuran-5-acetic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)benzofuran -5-acetic acid;

2-(2-(3-Phenyl-7-propylbenzofuran-6-yloxy)ethyl)-benzofuran-5-acetic acid;

2-(2-(4-Phenoxy-2-propylphenoxy)ethyl-4,5,6,7-tetrahydronaphtho[2,1-b]furan-7-carboxylic acid;

2-(2-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-4,5,6,7-tetrahydronaphtho[2,1-b]furan-7-carboxylic acid; and

2-(2-(3-(2,2-Dimethylpropyl)-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)-4,5,6,7-tetrahydronaphtho[2,1-b]furan-7-carboxylic acid

or a salt or hydrate thereof.

20. A compound according to Claim 19 which is:
2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid;

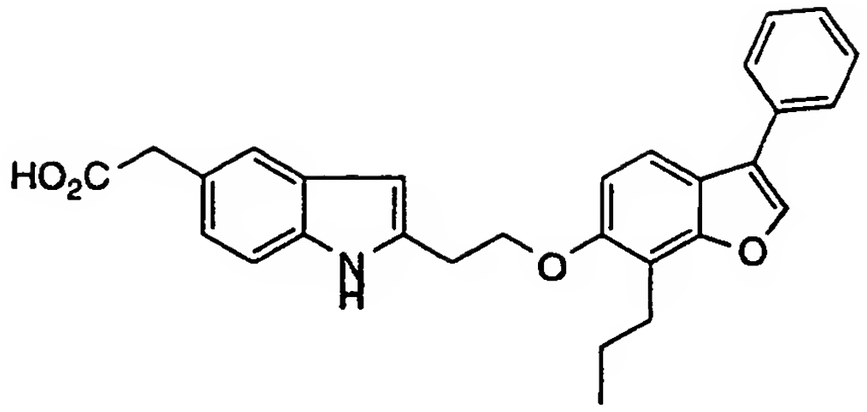
2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)indole-5-acetic acid methyl ester;

2-(2-(3-(2-Phenyl)ethyl-7-propylbenz[4,5]isoxazol-6-yloxy)ethyl)indole-5-acetic acid or

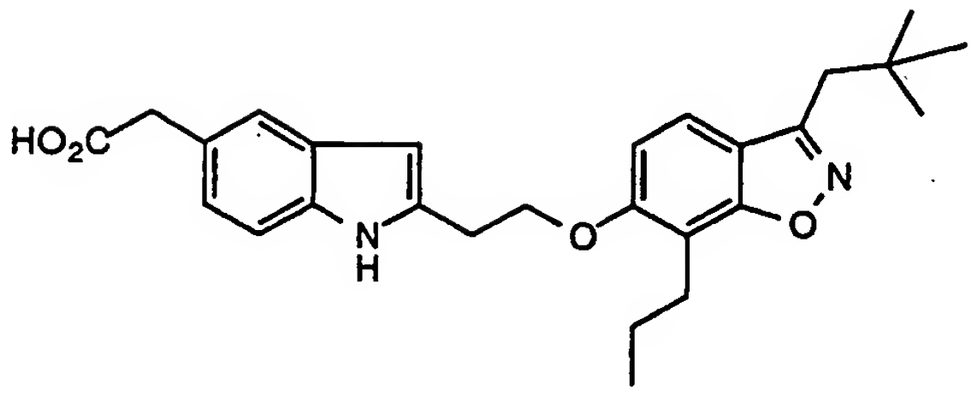
2-(2-(4-Phenoxy-2-propylphenoxy)ethyl)-4,5,6,7-tetrahydronaphtho[2,1-b]furan-7-carboxylic acid

or a salt or hydrate thereof.

21. A compound represented by one of the following structural formulas:



Ex 1



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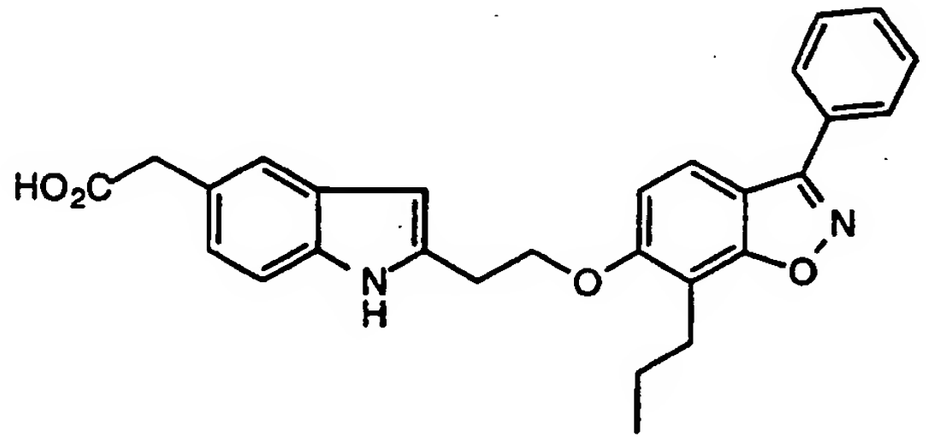

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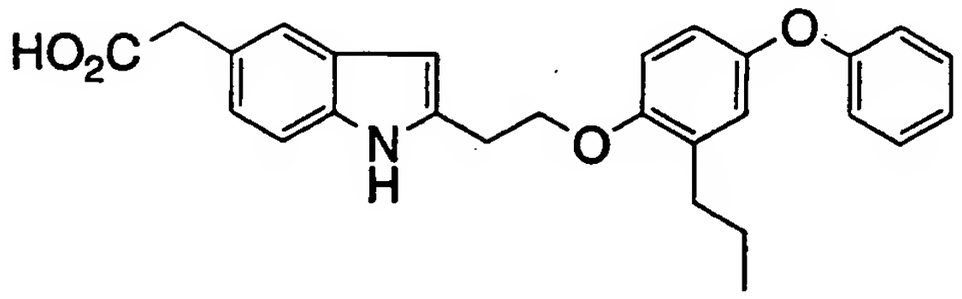

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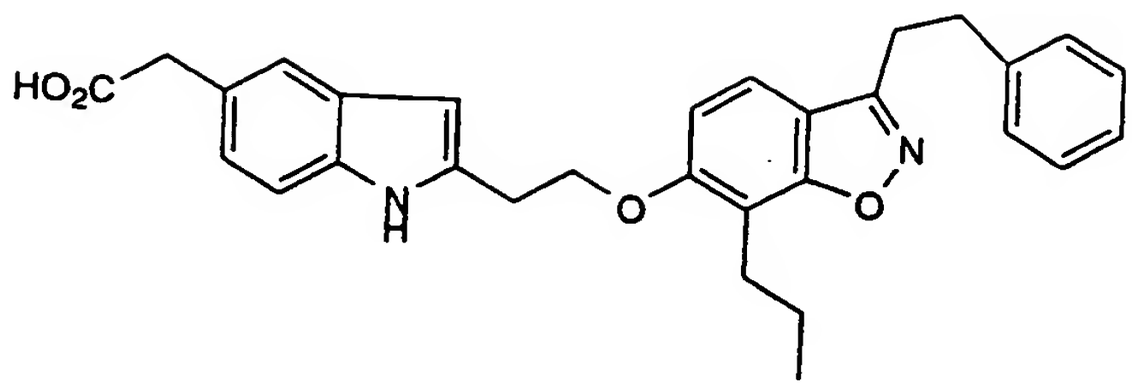

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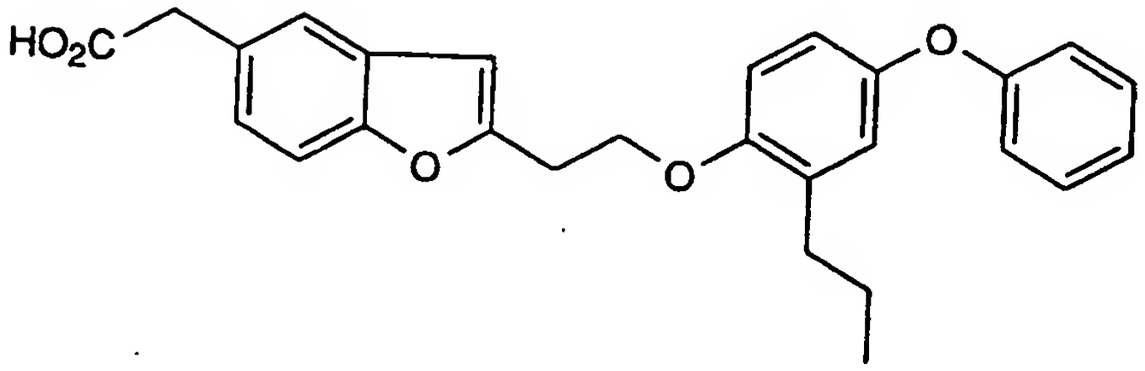

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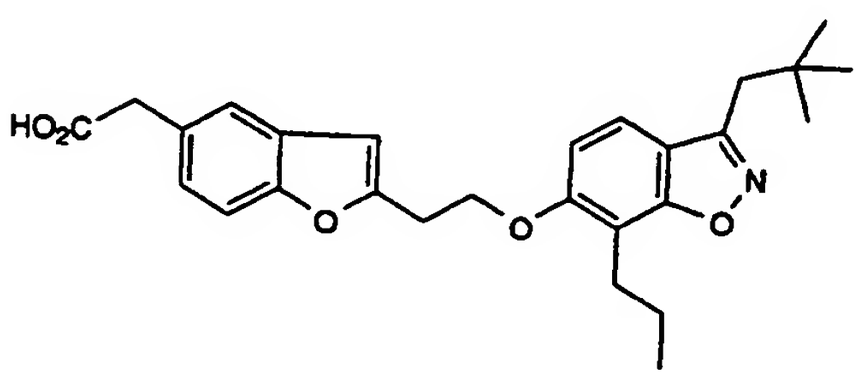

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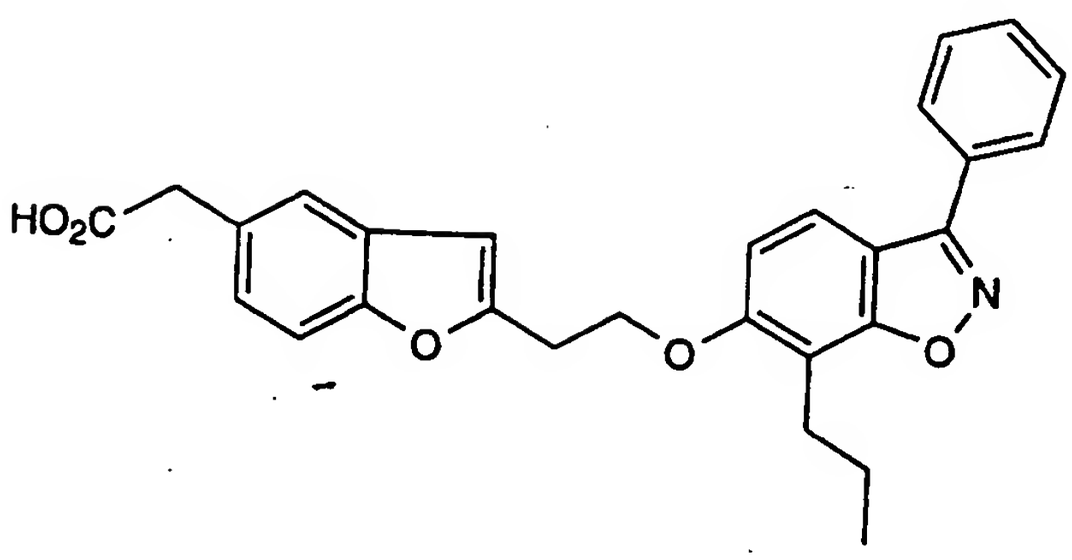

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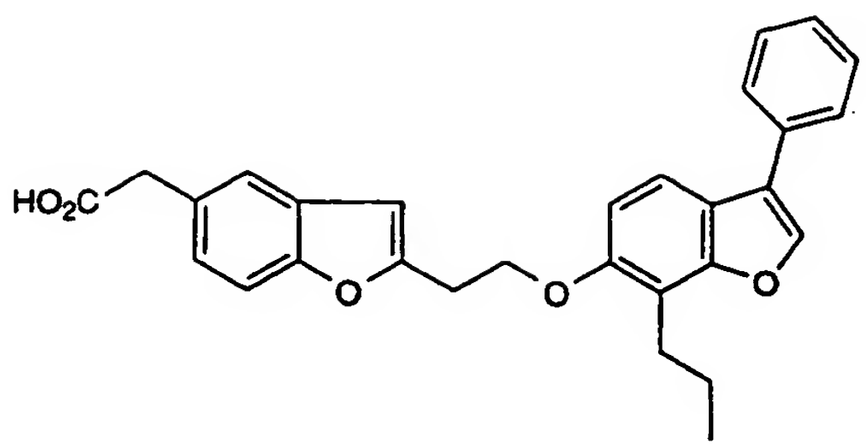
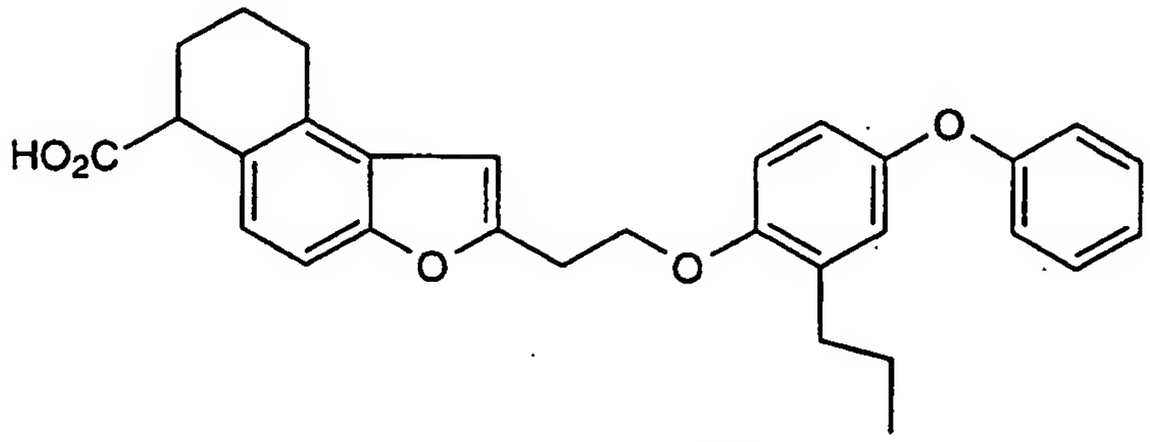


Ex 9



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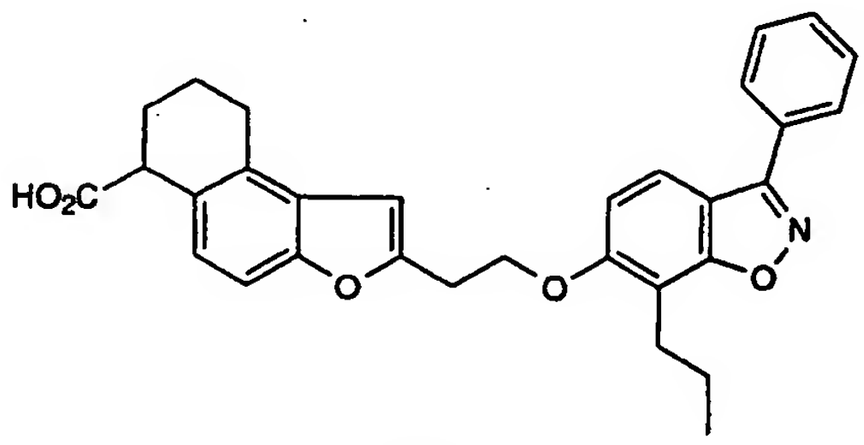

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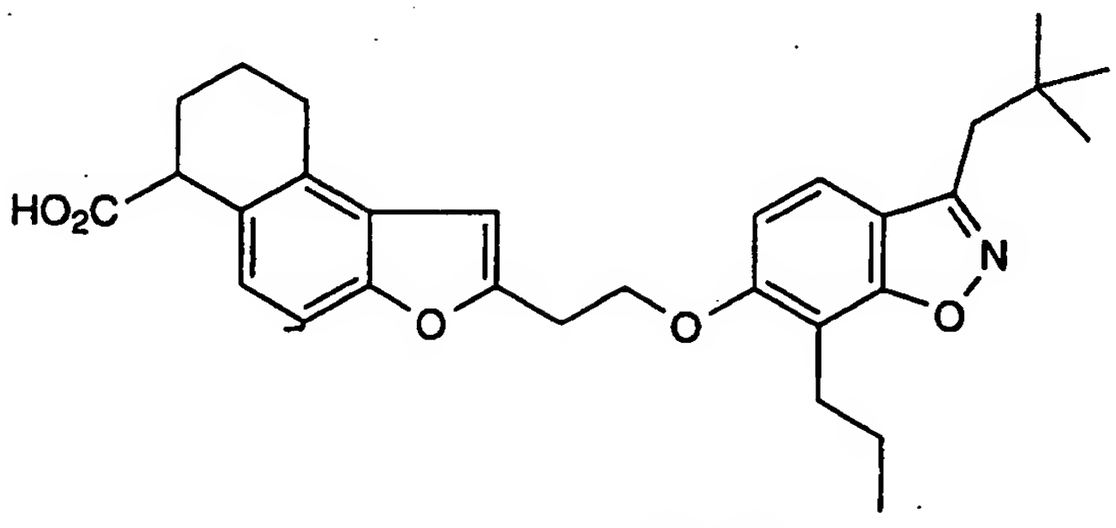

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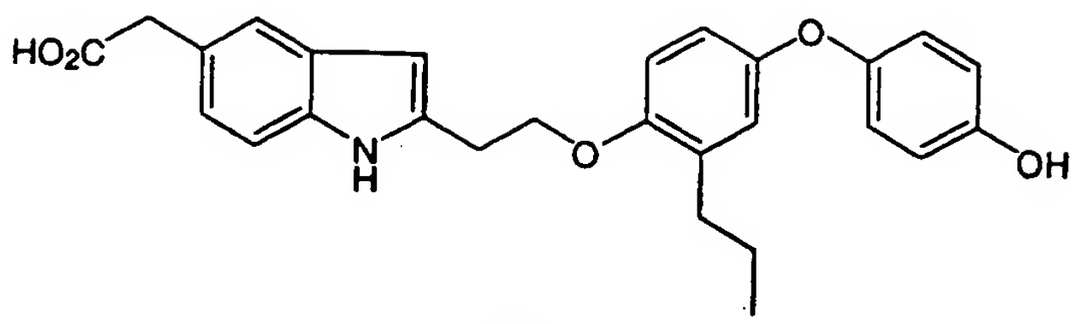
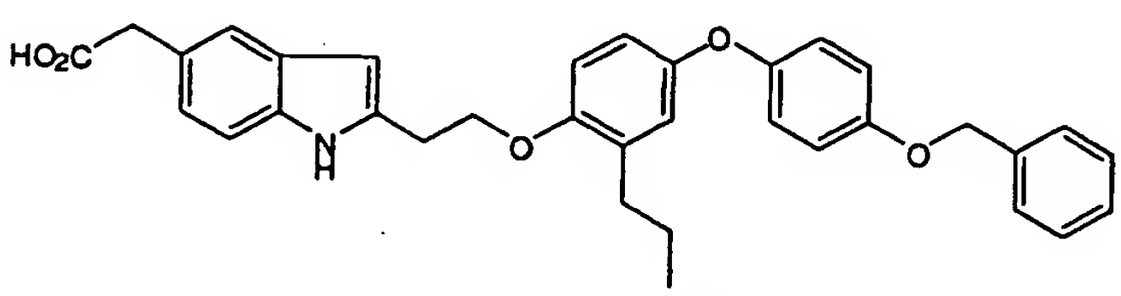
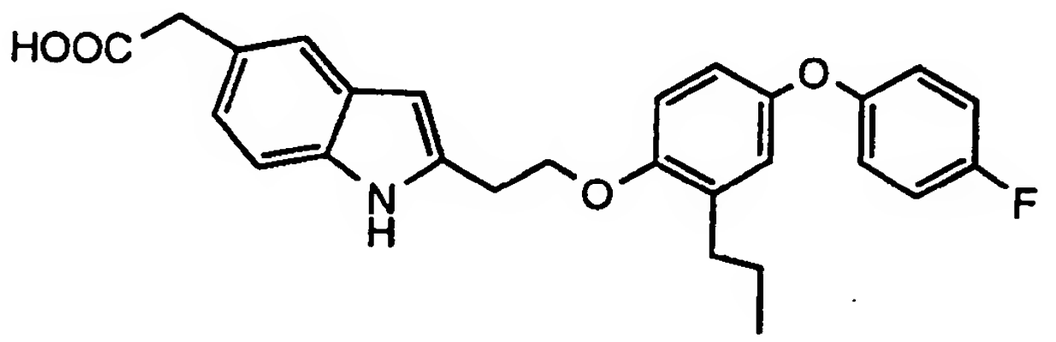


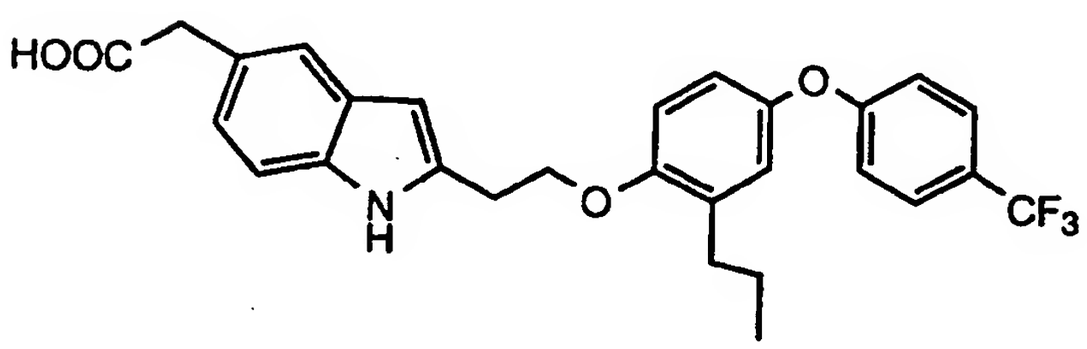
Ex 13



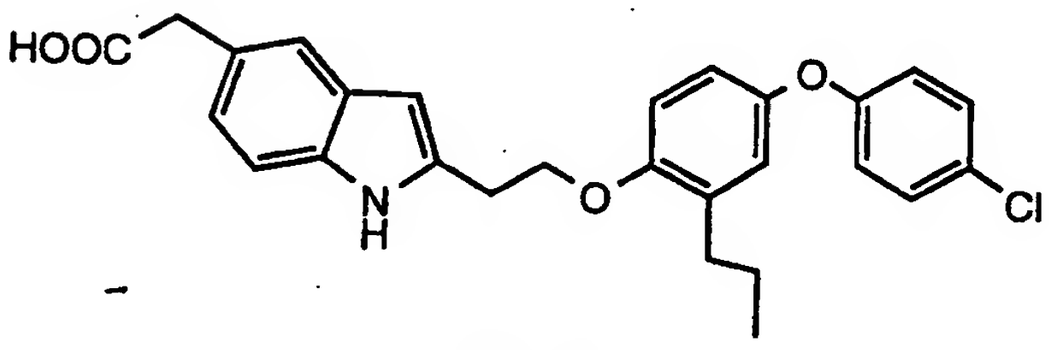
Ex 14



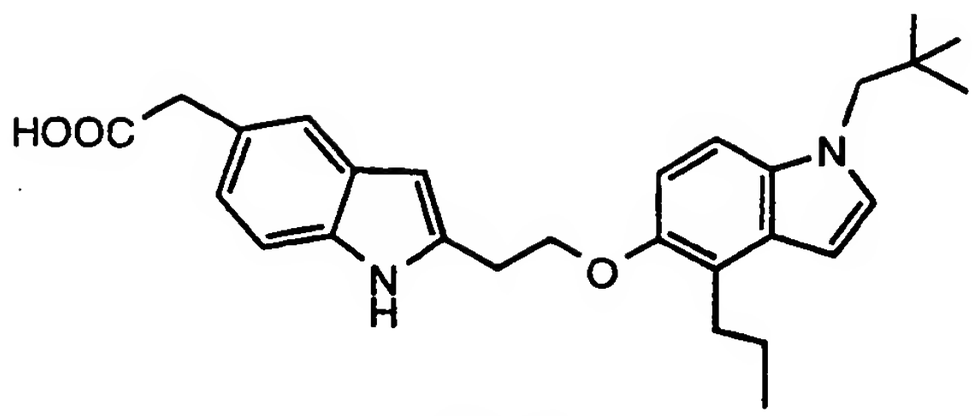
Ex 15



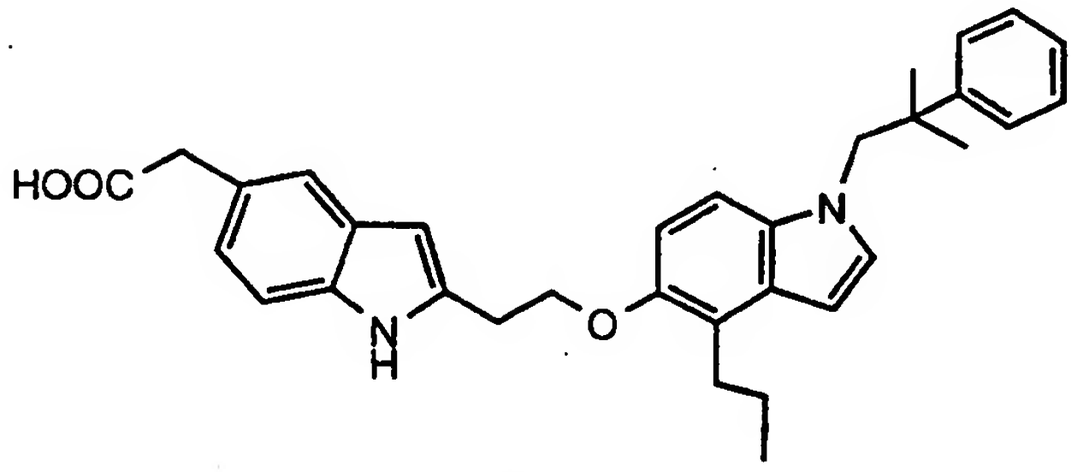
Ex 16



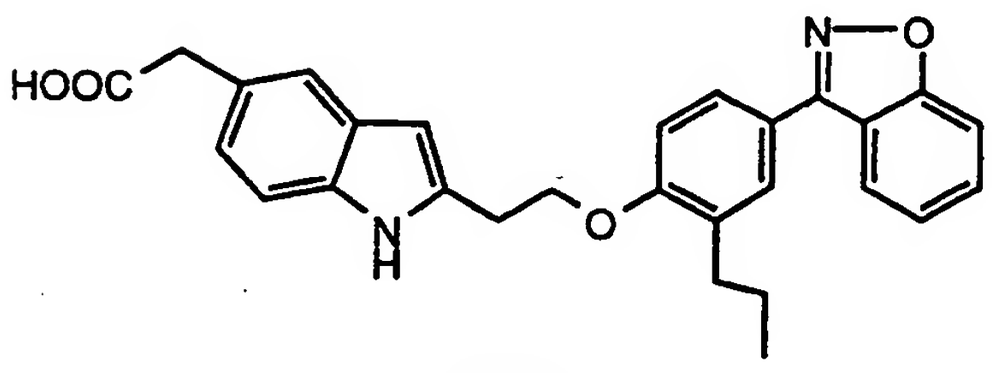
Ex 17



Ex 18



Ex 19



Ex 20

or a salt, ester or hydrate thereof.

22. Crystalline 2-(2-(4-Phenoxy-2-propylphenoxy)-ethyl)indole-5-acetic acid in accordance with claim 19, having an X-ray powder diffraction pattern in accordance with Table I:

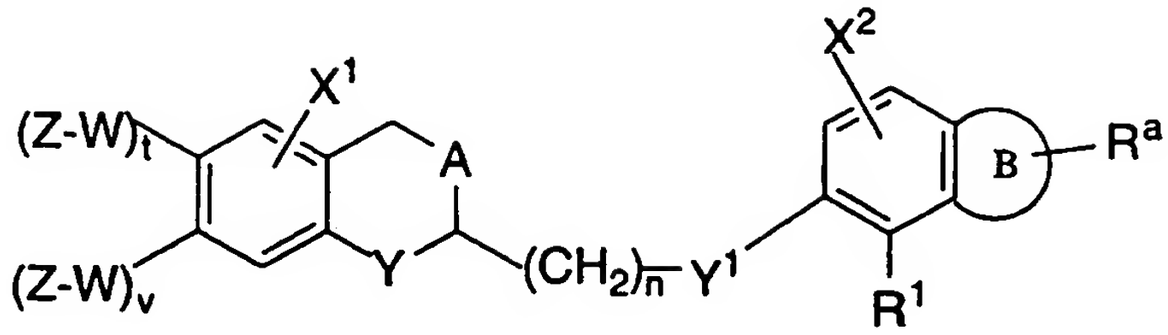
TABLE 1

Peak No.	Angle (deg)	Tip Width (deg)	Peak (cts)	Backg (cts)	D Spac (Ang)	I/Imax (%)	Type			Sign
							A1	A2	Ot	
1	8.3325	0.48	10.	6.	10.6028	2.34	x	x		0.83
2	9.7600	0.12	19.	7.	9.0550	4.43	x	x		0.89
3	12.1375	0.36	10.	8.	7.2861	2.34	x	x		1.05

4	14.1525	0.15	17.	9.	6.2529	3.85	x	x		0.91
5	16.1575	0.15	46.	12.	5.4812	10.59	x	x		2.09
6	16.6450	0.15	53.	12.	5.3218	12.20	x	x		1.02
7	16.8200	0.15	41.	12.	5.2668	9.38	x	x		0.91
8	17.6250	0.24	30.	13.	5.0280	6.93	x	x		1.26
9	18.2600	0.07	154.	13.	4.8546	35.20	x	x		1.38
10	18.9025	0.18	17.	14.	4.6910	3.85	x	x		1.26
11	19.5625	0.12	34.	14.	4.5342	7.70	x	x		0.76
12	20.5175	0.09	117.	15	4.3252	26.70	x	x		1.07
13	21.6225	0.21	48.	16	4.1066	10.90	x	x		2.88
14	22.6875	0.13	437.	17	3.9162	100.00	x	x		5.62
15	23.4200	0.09	128.	18	3.7954	29.23	x	x		0.78
16	23.8750	0.18	96.	18	3.7241	21.99	x	x		3.47
17	24.4900	0.12	72.	18	3.6319	16.54	x	x		3.02
18	25.0125	0.18	26.	18	3.5572	5.95	x	x		0.89
19	25.7275	0.18	20.	19	3.4599	4.64	x	x		0.83
20	26.6250	0.18	114.	20	3.3453	26.21	x	x		2.09
21	26.9725	0.09	246.	20	3.3030	56.43	x	x		1.74
22	27.9675	0.07	202.	21	3.1877	46.16	x	x		1.32
23	28.5925	0.24	30.	22	3.1194	6.93	x	x		1.05
24	30.8400	0.07	196.	24	2.8970	44.87	x	x		1.55
25	32.1275	0.18	38.	24	2.7838	8.80	x	x		1.82
26	32.6325	0.18	58.	25	2.7419	13.22	x	x		2.04
27	33.9250	0.18	174.	26	2.6403	39.89	x	x		5.13
28	35.1000	0.18	17.	27	2.5546	3.85	x	x		1.05
29	35.7950	0.24	32.	27	2.5065	7.44	x	x		3.16
30	36.8400	0.36	37.	28	2.4378	8.52	x	x		2.45
31	37.3975	0.15	35.	28	2.4027	7.97	x	x		1.07
32	37.8050	0.15	35.	28	2.3778	7.97	x	x		1.15
33	38.5300	0.12	69.	29	2.3347	15.77	x	x		1.15 .

23. Crystalline 2-(2-(4-Phenoxy-2-propylphenoxy)-ethyl)indole-5-acetic acid in accordance with claim 20 as the pentahydrate salt.

24. A method for the treatment or prevention of diabetes, diabetic retinopathy or diabetic nephropathy which comprises administering to a mammal in need of such treatment an anti-diabetic effective amount of a compound represented by formula I or Ia:



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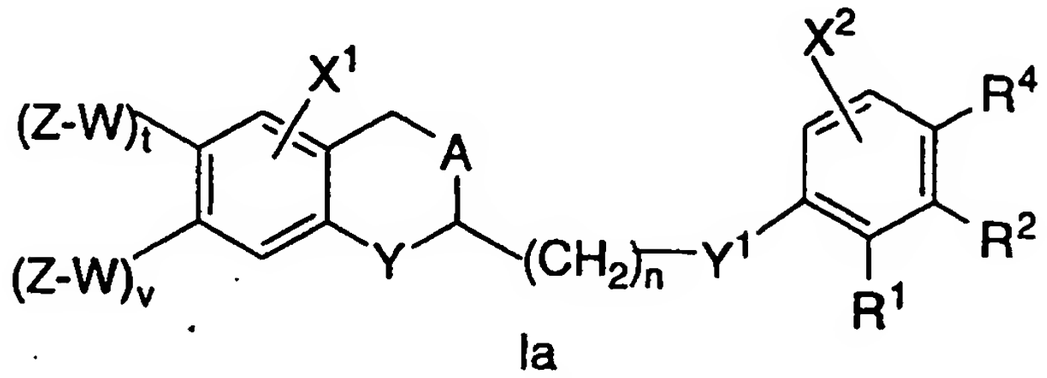


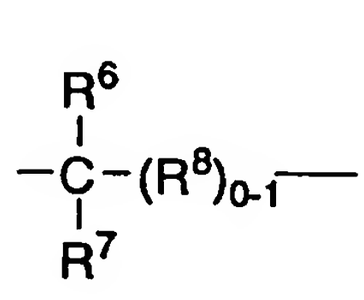
Ia

or a pharmaceutically acceptable salt thereof, wherein:

A represents a single or double bonded carbon, or a direct single or double bond;

Y represents a member selected from the group consisting of: $-S(O)_p-$ wherein p is 0, 1 or 2, , $-CH_2-$, -C(O)- , $-NR^1-$, -O-, $-SO_2NH-$ and
$-NHSO_2-$;

one of t and v is zero and the other is 1;



W is , and

Z is selected from the group consisting of: $CO_2R^{3'}$, $CONHSO_2C_{1-6}$ alkyl, $CONH_2$ and 5-(1H-tetrazolyl); or in the alternative,

one of $(Z\text{-}W)_t$ and $(Z\text{-}W)_v$ is taken in combination with X^1 to represent a 5 or 6 membered fused ring, said ring being a carbocycle, aryl or heteroaryl ring, and being optionally substituted with 1 to 3 R^a groups;

when $(Z\text{-}W)_t$ is taken in combination with X^1, v is 0 or 1, and when $(Z\text{-}W)_v$ is taken in combination with X^1, t is 0 or 1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{2\text{-}15}$ alkynyl, halo, $C_{5\text{-}10}$ aryl, $C_{5\text{-}10}$ heteroaryl, $C_{1\text{-}10}$ acyl, $C_{1\text{-}5}$ alkoxy, $C_{5\text{-}10}$ aryloxy, $C_{2\text{-}15}$ alkenyloxy, $C_{2\text{-}15}$ alkynyloxy, heteroaryloxy, $C_{1\text{-}10}$ acyloxy

said alkyl, alkenyl, alkynyl, aryl, acyl and heteroaryl, and the alkyl, alkenyl, alkynyl, aryl acy and heteroaryl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

n is 2, 3 or 4;

Y^1 represents O, NH, CH_2 or $S(O)_p$ wherein p is as defined above;

B represents a 5 or 6 membered fused ring containing 0 to 2 double bonds, and optionally containing 1 to 3 heteroatoms selected from the group consisting of O, S and N, said ring being optionally substituted with 1 to 3 R^a groups;

R^1 is selected from a group consisting of: H, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl and $C_{2\text{-}15}$ alkynyl, said alkyl, alkenyl and alkynyl being optionally substituted with 1 to 3 R^a groups;

R^2 is selected from a group consisting of: H, OH, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{2\text{-}15}$ alkynyl, $C_{5\text{-}10}$ aryl, $C_{5\text{-}10}$ heteroaryl, $-C(O)C_{1\text{-}15}$ alkyl, $CO_2C_{1\text{-}6}$ alkyl, $-OC(O)R^{3'}$, $C_{1\text{-}6}$ alkoxy, $C_{5\text{-}10}$ aryloxy, $C_{2\text{-}15}$ alkenyloxy, $C_{2\text{-}15}$ alkynyloxy, heteroaryloxy and $C_{1\text{-}10}$ acyloxy,

said alkyl, alkenyl, alkynyl, aryl and heteroaryl, and the alkyl, aryl, alkenyl, alkynyl heteroaryl and acyl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

R^3 is selected from a group consisting of: H, OH, NHR^1, NHacyl, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{1\text{-}15}$ alkoxy, CO_2alkyl, $C_{2\text{-}15}$

alkynyl, C_{5-10} aryl, and C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 R^a groups;

each R^a independently represents a member selected from the group consisting of: $R^{3'}$, halo, CF_3, OCF_3, CN, NO_2, , $OR^{3'}$, $S(O)_p$-$R^{3'}$; $N(R^{3'})_2$, $NR^{3'}COR^{3'}$, $NR^{3'}CO_2R^{3'}$, $NR^{3'}CON(R^{3'})_2$, $NR^{3'}SO_2R^{3'}$, $C(O)R^{3'}$, $CO_2R^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, $OCON(R^{3'})_2$, and when $R^{3'}$ is present and represents alkyl, alkenyl, alkynyl, aryl or heteroaryl, said alkyl, alkenyl, alkynyl, aryl or heteroaryl group is optionally substituted with 1 to 3 halo, hydroxy, C_{1-3} alkoxy, carboxy or amino groups, and

when at least two R^a groups are present, they may also be taken in combination with any intervening atoms to represent a 4-6 membered ring, said ring containing 0-3 heteroatoms selected from O, $S(O)_p$ and N, and said ring being optionally interrupted by 1-2 -C(O)- groups, and optionally substituted with 1-3 halo, hydroxy, C_{1-6} alkyl or amino groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl;

R^4 represents R^2, -D-R^5 or $\sim C(R^3)=Y^2$;

D is selected from O, S(O)p ,NR^1 and CR^6R^7;

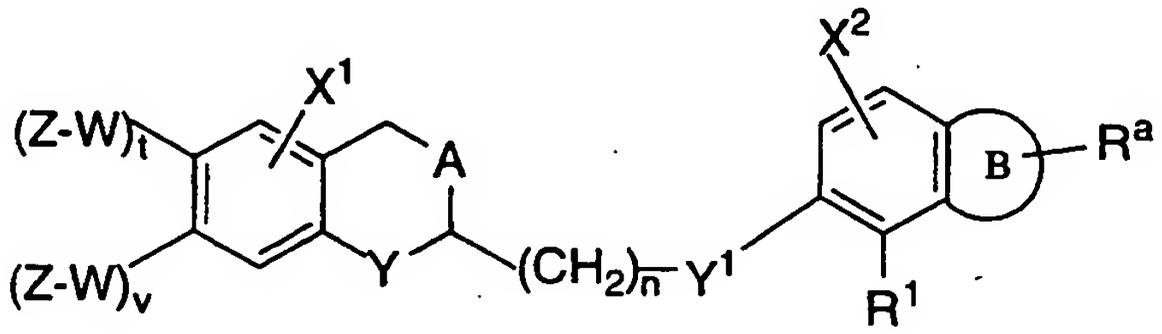
R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl being optionally substituted with 1 to 3 R^a groups;

Y^2 is selected from the group consisting of: O, $N(C_{1-15})$ alkyl, $N(CO_2)$alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 then n is 2;

R^8 is optional and is selected from the group consisting of CR^6R^7, O, NR^6 and $S(O)_p$,

and R^6 and R^7 are independently selected from H and C_{1-6} alkyl.

25. A method of lowering triglyceride levels in a mammalian patient in need of such treatment, which comprises administering to said patient a triglyceride lowering effective amount of a compound represented by formula I or Ia:



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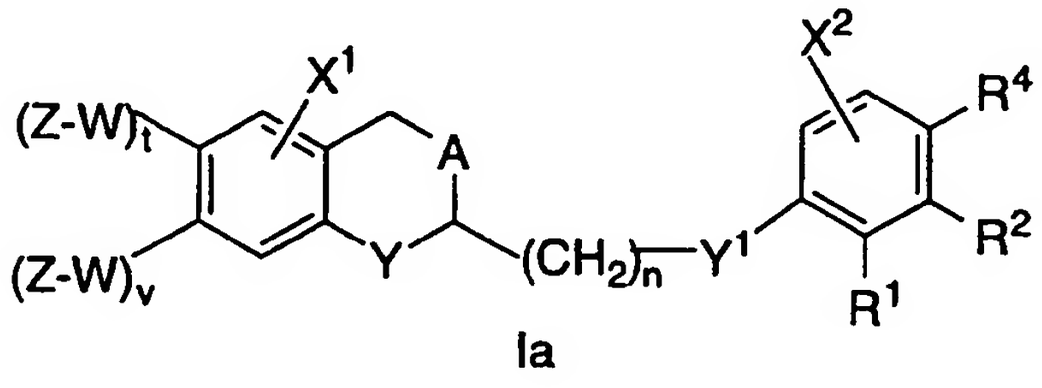


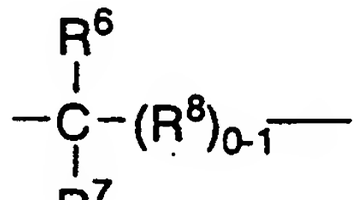
Ia

or a pharmaceutically acceptable salt thereof, wherein:

A represents a single or double bonded carbon, or a direct single or double bond;

Y represents a member selected from the group consisting of: $-S(O)_p-$ wherein p is 0, 1 or 2, , $-CH_2-$, -C(O)- , $-NR^1-$, -O-, $-SO_2NH-$ and
$-NHSO_2-$;

one of t and v is zero and the other is 1;

W is  , and

Z is selected from the group consisting of: $CO_2R^{3'}$, $CONHSO_2C_{1-6}$ alkyl, $CONH_2$ and 5-(1H-tetrazolyl); or in the alternative,

one of $(Z\text{-}W)_t$ and $(Z\text{-}W)_v$ is taken in combination with X^1 to represent a 5 or 6 membered fused ring, said ring being a carbocycle, aryl or heteroaryl ring, and being optionally substituted with 1 to 3 R^a groups;

when $(Z\text{-}W)_t$ is taken in combination with X^1, v is 0 or 1, and when $(Z\text{-}W)_v$ is taken in combination with X^1, t is 0 or 1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, halo, C_{5-10} aryl, C_{5-10} heteroaryl, C_{1-10} acyl, C_{1-5} alkoxy, C_{5-10} aryloxy, C_{2-15} alkenyloxy, C_{2-15} alkynyloxy, heteroaryloxy, C_{1-10} acyloxy

said alkyl, alkenyl, alkynyl, aryl, acyl and heteroaryl, and the alkyl, alkenyl, alkynyl, aryl acy and heteroaryl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

n is 2, 3 or 4;

Y^1 represents O, NH, CH_2 or $S(O)_p$ wherein p is as defined above;

B represents a 5 or 6 membered fused ring containing 0 to 2 double bonds, and optionally containing 1 to 3 heteroatoms selected from the group consisting of O, S and N, said ring being optionally substituted with 1 to 3 R^a groups;

R^1 is selected from a group consisting of: H, C_{1-15} alkyl, C_{2-15} alkenyl and C_{2-15} alkynyl, said alkyl, alkenyl and alkynyl being optionally substituted with 1 to 3 R^a groups;

R^2 is selected from a group consisting of: H, OH, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, C_{5-10} aryl, C_{5-10} heteroaryl, $-C(O)C_{1-}$

15 alkyl, CO_2C_{1-6} alkyl, $-OC(O)R^{3'}$, C_{1-6} alkoxy, C_{5-10} aryloxy, C_{2-15} alkenyloxy, C_{2-15} alkynyloxy, heteroaryloxy and C_{1-10} acyloxy,

said alkyl, alkenyl, alkynyl, aryl and heteroaryl, and the alkyl, aryl, alkenyl, alkynyl heteroaryl and acyl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

R^3 is selected from a group consisting of: H, OH, NHR^1, NHacyl, C_{1-15} alkyl, C_{2-15} alkenyl, C_{1-15} alkoxy, CO_2alkyl, C_{2-15} alkynyl, C_{5-10} aryl, and C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 R^a groups;

each R^a independently represents a member selected from the group consisting of: $R^{3'}$, halo, CF_3, OCF_3, CN, NO_2, , $OR^{3'}$, $S(O)_p$-$R^{3'}$; $N(R^{3'})_2$, $NR^{3'}COR^{3'}$, $NR^{3'}CO_2R^{3'}$, $NR^{3'}CON(R^{3'})_2$, $NR^{3'}SO_2R^{3'}$, $C(O)R^{3'}$, $CO_2R^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, $OCON(R^{3'})_2$, and when $R^{3'}$ is present and represents alkyl, alkenyl, alkynyl, aryl or heteroaryl, said alkyl, alkenyl, alkynyl, aryl or heteroaryl group is optionally substituted with 1 to 3 halo, hydroxy, C_{1-3} alkoxy, carboxy or amino groups, and

when at least two R^a groups are present, they may also be taken in combination with any intervening atoms to represent a 4-6 membered ring, said ring containing 0-3 heteroatoms selected from O, $S(O)_p$ and N, and said ring being optionally interrupted by 1-2 -C(O)- groups, and optionally substituted with 1-3 halo, hydroxy, C_{1-6} alkyl or amino groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl;

R^4 represents R^2, $-D-R^5$ or ;

D is selected from O, S(O)p ,NR^1 and CR^6R^7;

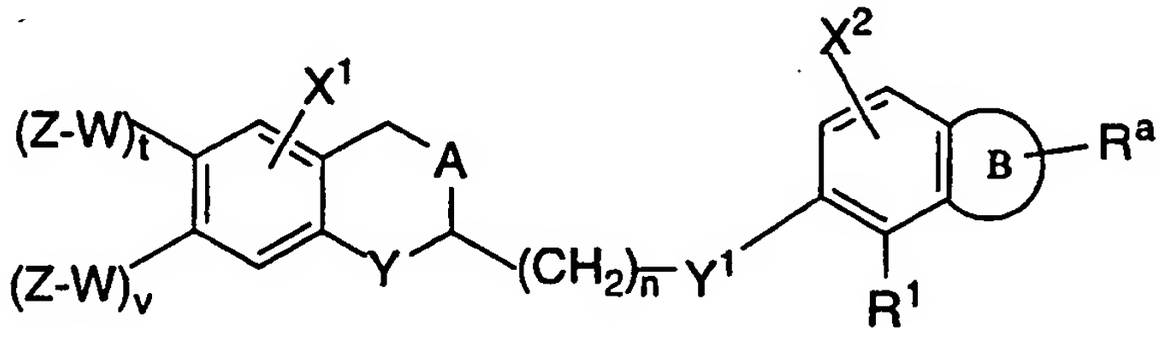
R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl being optionally substituted with 1 to 3 R^a groups;

Y^2 is selected from the group consisting of: O, $N(C_{1-15})$ alkyl, $N(CO_2)$alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 then n is 2;

R^8 is optional and is selected from the group consisting of CR^6R^7, O, NR^6 and $S(O)_p$,

and R^6 and R^7 are independently selected from H and C_{1-6} alkyl.

26. A method for treating obesity in a mammalian patient in need of such treatment which comprises administering to said patient an effective amount of a compound represented by formula I or Ia:



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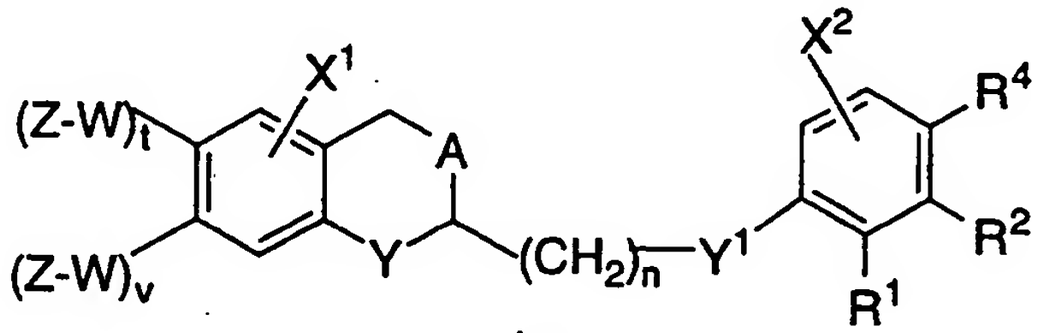


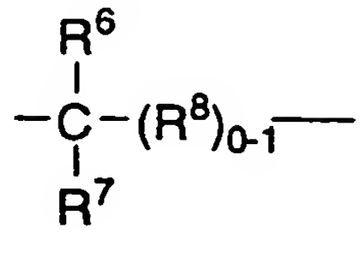
Ia

or a pharmaceutically acceptable salt thereof, wherein:

A represents a single or double bonded carbon, or a direct single or double bond;

Y represents a member selected from the group consisting of: $-S(O)_p-$ wherein p is 0, 1 or 2, , $-CH_2-$, -C(O)- , $-NR^1-$, -O-, $-SO_2NH-$ and
$-NHSO_2-$;

one of t and v is zero and the other is 1;

W is  , and

Z is selected from the group consisting of: $CO_2R^{3'}$, $CONHSO_2C_{1-6}$ alkyl, $CONH_2$ and 5-(1H-tetrazolyl); or in the alternative,

one of $(Z\text{-}W)_t$ and $(Z\text{-}W)_v$ is taken in combination with X^1 to represent a 5 or 6 membered fused ring, said ring being a carbocycle, aryl or heteroaryl ring, and being optionally substituted with 1 to 3 R^a groups;

when $(Z\text{-}W)_t$ is taken in combination with X^1, v is 0 or 1, and when $(Z\text{-}W)_v$ is taken in combination with X^1, t is 0 or 1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, halo, C_{5-10} aryl, C_{5-10} heteroaryl, C_{1-10} acyl, C_{1-5} alkoxy, C_{5-10} aryloxy, C_{2-15} alkenyloxy, C_{2-15} alkynyloxy, heteroaryloxy, C_{1-10} acyloxy

said alkyl, alkenyl, alkynyl, aryl, acyl and heteroaryl, and the alkyl, alkenyl, alkynyl, aryl acy and heteroaryl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

n is 2, 3 or 4;

Y^1 represents O, NH, CH_2 or $S(O)_p$ wherein p is as defined above;

B represents a 5 or 6 membered fused ring containing 0 to 2 double bonds, and optionally containing 1 to 3 heteroatoms selected from the group consisting of O, S and N, said ring being optionally substituted with 1 to 3 R^a groups;

R^1 is selected from a group consisting of: H, C_{1-15} alkyl, C_{2-15} alkenyl and C_{2-15} alkynyl, said alkyl, alkenyl and alkynyl being optionally substituted with 1 to 3 R^a groups;

R^2 is selected from a group consisting of: H, OH, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, C_{5-10} aryl, C_{5-10} heteroaryl, -$C(O)C_{1-15}$ alkyl, CO_2C_{1-6} alkyl, -$OC(O)R^{3'}$, C_{1-6} alkoxy, C_{5-10} aryloxy, C_{2-15} alkenyloxy, C_{2-15} alkynyloxy, heteroaryloxy and C_{1-10} acyloxy,

said alkyl, alkenyl, alkynyl, aryl and heteroaryl, and the alkyl, aryl, alkenyl, alkynyl heteroaryl and acyl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

R^3 is selected from a group consisting of: H, OH, NHR^1, NHacyl, C_{1-15} alkyl, C_{2-15} alkenyl, C_{1-15} alkoxy, CO_2alkyl, C_{2-15} alkynyl, C_{5-10} aryl, and C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 R^a groups;

each R^a independently represents a member selected from the group consisting of: $R^{3'}$, halo, CF_3, OCF_3, CN, NO_2, , $OR^{3'}$, $S(O)_p$-$R^{3'}$; $N(R^{3'})_2$, $NR^{3'}COR^{3'}$, $NR^{3'}CO_2R^{3'}$, $NR^{3'}CON(R^{3'})_2$, $NR^{3'}SO_2R^{3'}$, $C(O)R^{3'}$, $CO_2R^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, $OCON(R^{3'})_2$, and when $R^{3'}$ is present and represents alkyl, alkenyl, alkynyl, aryl or heteroaryl, said alkyl, alkenyl, alkynyl, aryl or heteroaryl group is optionally substituted with 1 to 3 halo, hydroxy, C_{1-3} alkoxy, carboxy or amino groups, and

when at least two R^a groups are present, they may also be taken in combination with any intervening atoms to represent a 4-6 membered ring, said ring containing 0-3 heteroatoms selected from O, $S(O)_p$ and N, and said ring being optionally interrupted by 1-2 -C(O)- groups, and optionally substituted with 1-3 halo, hydroxy, C_{1-6} alkyl or amino groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl;

R^4 represents R^2, -D-R^5 or ;

D is selected from O, S(O)p ,NR^1 and CR^6R^7;

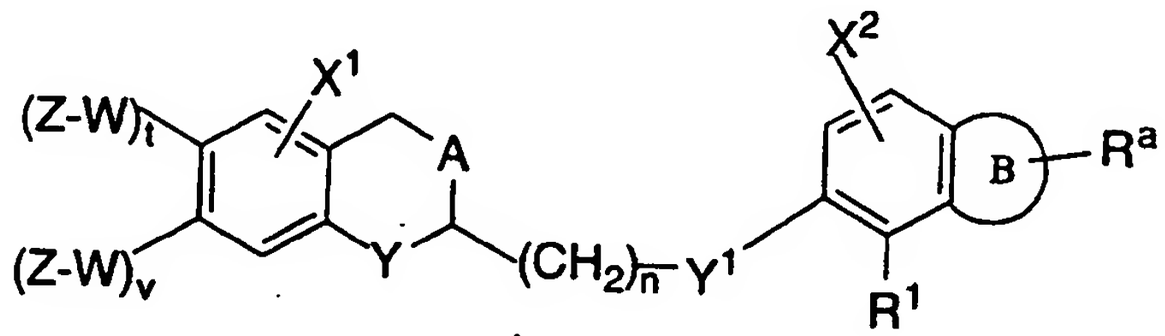
R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl being optionally substituted with 1 to 3 R^a groups;

Y^2 is selected from the group consisting of: O, N(C_{1-15}) alkyl, N(CO_2)alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 then n is 2;

R^8 is optional and is selected from the group consisting of CR^6R^7, O, NR^6 and $S(O)_p$,

and R^6 and R^7 are independently selected from H and C_{1-6} alkyl.

27. A method for halting, preventing or reducing the risk of developing atherosclerosis and related diseae events in a patient in need of such treatment, comprising the administration of an anti-atherosclerotic effective amount of a compound represented by formula I or Ia:



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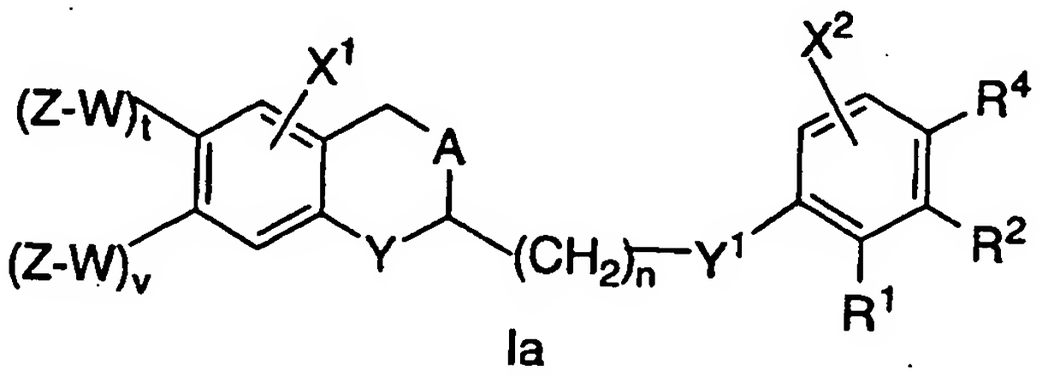


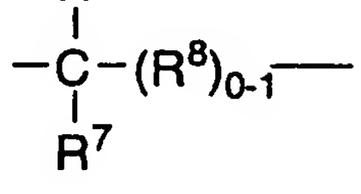
Ia

or a pharmaceutically acceptable salt thereof, wherein:

A represents a single or double bonded carbon, or a direct single or double bond;

Y represents a member selected from the group consisting of: $-S(O)_p-$ wherein p is 0, 1 or 2, , $-CH_2-$, -C(O)- , $-NR^1-$, -O-, $-SO_2NH-$ and $-NHSO_2-$;

one of t and v is zero and the other is 1;

W is  , and

Z is selected from the group consisting of: $CO_2R^{3'}$, $CONHSO_2C_{1-6}$ alkyl, $CONH_2$ and 5-(1H-tetrazolyl); or in the alternative,

one of $(Z\text{-}W)_t$ and $(Z\text{-}W)_v$ is taken in combination with X^1 to represent a 5 or 6 membered fused ring, said ring being a carbocycle, aryl or heteroaryl ring, and being optionally substituted with 1 to 3 R^a groups;

when $(Z\text{-}W)_t$ is taken in combination with X^1, v is 0 or 1, and when $(Z\text{-}W)_v$ is taken in combination with X^1, t is 0 or 1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, halo, C_{5-10} aryl, C_{5-10} heteroaryl, C_{1-10} acyl, C_{1-5} alkoxy, C_{5-10} aryloxy, C_{2-15} alkenyloxy, C_{2-15} alkynyloxy, heteroaryloxy, C_{1-10} acyloxy

said alkyl, alkenyl, alkynyl, aryl, acyl and heteroaryl, and the alkyl, alkenyl, alkynyl, aryl acy and heteroaryl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

n is 2, 3 or 4;

Y^1 represents O, NH, CH_2 or $S(O)_p$ wherein p is as defined above;

B represents a 5 or 6 membered fused ring containing 0 to 2 double bonds, and optionally containing 1 to 3 heteroatoms selected from the group consisting of O, S and N, said ring being optionally substituted with 1 to 3 R^a groups;

R^1 is selected from a group consisting of: H, C_{1-15} alkyl, C_{2-15} alkenyl and C_{2-15} alkynyl, said alkyl, alkenyl and alkynyl being optionally substituted with 1 to 3 R^a groups;

R^2 is selected from a group consisting of: H, OH, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, C_{5-10} aryl, C_{5-10} heteroaryl, -$C(O)C_{1-15}$ alkyl, CO_2C_{1-6} alkyl, -$OC(O)R^{3'}$, C_{1-6} alkoxy, C_{5-10} aryloxy, C_{2-15} alkenyloxy, C_{2-15} alkynyloxy, heteroaryloxy and C_{1-10} acyloxy,

said alkyl, alkenyl, alkynyl, aryl and heteroaryl, and the alkyl, aryl, alkenyl, alkynyl heteroaryl and acyl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

R^3 is selected from a group consisting of: H, OH, NHR^1, NHacyl, C_{1-15} alkyl, C_{2-15} alkenyl, C_{1-15} alkoxy, CO_2alkyl, C_{2-15} alkynyl, C_{5-10} aryl, and C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 R^a groups;

each R^a independently represents a member selected from the group consisting of: $R^{3'}$, halo, CF_3, OCF_3, CN, NO_2, , $OR^{3'}$, $S(O)_p$-$R^{3'}$; $N(R^{3'})_2$, $NR^{3'}COR^{3'}$, $NR^{3'}CO_2R^{3'}$, $NR^{3'}CON(R^{3'})_2$, $NR^{3'}SO_2R^{3'}$, $C(O)R^{3'}$, $CO_2R^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, $OCON(R^{3'})_2$, and when $R^{3'}$ is present and represents alkyl, alkenyl, alkynyl, aryl or heteroaryl, said alkyl, alkenyl, alkynyl, aryl or heteroaryl group is optionally substituted with 1 to 3 halo, hydroxy, C_{1-3} alkoxy, carboxy or amino groups, and

when at least two R^a groups are present, they may also be taken in combination with any intervening atoms to represent a 4-6 membered ring, said ring containing 0-3 heteroatoms selected from O, $S(O)_p$ and N, and said ring being optionally interrupted by 1-2 -C(O)-

groups, and optionally substituted with 1-3 halo, hydroxy, C_{1-6} alkyl or amino groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl;

R^4 represents R^2, -D-R^5 or $\sim C(R^3)=Y^2$;

D is selected from O, S(O)p ,NR^1 and CR^6R^7;

R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl being optionally substituted with 1 to 3 R^a groups;

Y^2 is selected from the group consisting of: O, N(C_{1-15}) alkyl, N(CO_2)alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 then n is 2;

R^8 is optional and is selected from the group consisting of CR^6R^7, O, NR^6 and $S(O)_p$,

and R^6 and R^7 are independently selected from H and C_{1-6} alkyl.

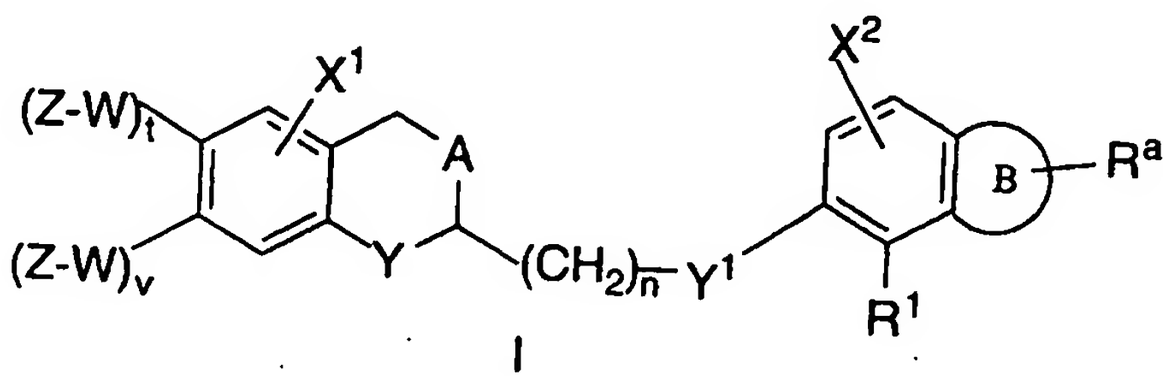
28. A method according to claim 24 wherein the compound has an IC_{50} equal to or less than 10 μM in the hPPARδ binding assay.

29. The method of Claim 25 wherein the compound has an IC_{50} equal to or less than 100 nM in the hPPARδ binding assay.

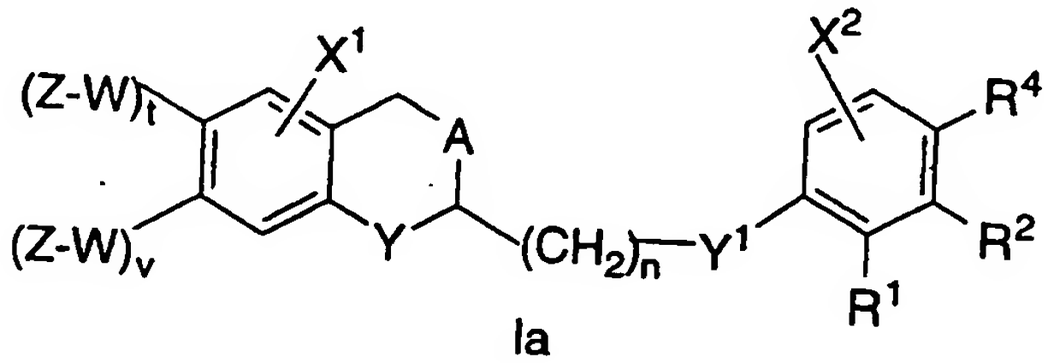
30. The method of Claim 26 wherein the compound has an IC_{50} equal to or less than 50 nM in the hPPARδ binding assay.

31. The method of Claim 27 wherein the compound has an IC_{50} equal to or less than 10 nM in the hPPARδ binding assay.

32. A method for raising high densisty lipoprotein plasma levels in a patient in need of such treatment, comprising the administration of a pharmaceutically effective amount of a compound represented by formula I or Ia:



I



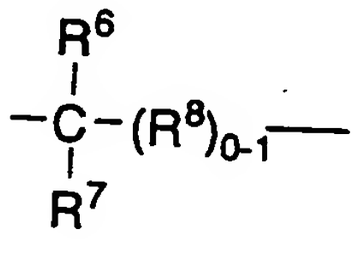
Ia

or a pharmaceutically acceptable salt thereof, wherein:

A represents a single or double bonded carbon, or a direct single or double bond;

Y represents a member selected from the group consisting of: $-S(O)_p-$ wherein p is 0, 1 or 2, , $-CH_2-$, -C(O)- , $-NR^1-$, -O-, $-SO_2NH-$ and
$-NHSO_2-$;

one of t and v is zero and the other is 1;

W is  , and

Z is selected from the group consisting of: $CO_2R^{3'}$, $CONHSO_2C_{1-6}$ alkyl, $CONH_2$ and 5-(1H-tetrazolyl); or in the alternative,

one of $(Z\text{-}W)_t$ and $(Z\text{-}W)_v$ is taken in combination with X^1 to represent a 5 or 6 membered fused ring, said ring being a carbocycle, aryl or heteroaryl ring, and being optionally substituted with 1 to 3 R^a groups;

when $(Z\text{-}W)_t$ is taken in combination with X^1, v is 0 or 1, and when $(Z\text{-}W)_v$ is taken in combination with X^1, t is 0 or 1;

X^1 and X^2 are independently selected from a group consisting of: H, OH, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{2\text{-}15}$ alkynyl, halo, $C_{5\text{-}10}$ aryl, $C_{5\text{-}10}$ heteroaryl, $C_{1\text{-}10}$ acyl, $C_{1\text{-}5}$ alkoxy, $C_{5\text{-}10}$ aryloxy, $C_{2\text{-}15}$ alkenyloxy, $C_{2\text{-}15}$ alkynyloxy, heteroaryloxy, $C_{1\text{-}10}$ acyloxy

said alkyl, alkenyl, alkynyl, aryl, acyl and heteroaryl, and the alkyl, alkenyl, alkynyl, aryl acy and heteroaryl portions of alkoxy, aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

n is 2, 3 or 4;

Y^1 represents O, NH, CH_2 or $S(O)_p$ wherein p is as defined above;

B represents a 5 or 6 membered fused ring containing 0 to 2 double bonds, and optionally containing 1 to 3 heteroatoms selected from the group consisting of O, S and N, said ring being optionally substituted with 1 to 3 R^a groups;

R^1 is selected from a group consisting of: H, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl and $C_{2\text{-}15}$ alkynyl, said alkyl, alkenyl and alkynyl being optionally substituted with 1 to 3 R^a groups;

R^2 is selected from a group consisting of: H, OH, $C_{1\text{-}15}$ alkyl, $C_{2\text{-}15}$ alkenyl, $C_{2\text{-}15}$ alkynyl, $C_{5\text{-}10}$ aryl, $C_{5\text{-}10}$ heteroaryl, $-C(O)C_{1\text{-}15}$ alkyl, $CO_2C_{1\text{-}6}$ alkyl, $-OC(O)R^{3'}$, $C_{1\text{-}6}$ alkoxy, $C_{5\text{-}10}$ aryloxy, $C_{2\text{-}15}$ alkenyloxy, $C_{2\text{-}15}$ alkynyloxy, heteroaryloxy and $C_{1\text{-}10}$ acyloxy,

said alkyl, alkenyl, alkynyl, aryl and heteroaryl, and the alkyl, aryl, alkenyl, alkynyl heteroaryl and acyl portions of alkoxy,

aryloxy, alkenyloxy, alkynyloxy, heteroaryloxy and acyloxy being optionally substituted with 1 to 3 R^a groups;

R^3 is selected from a group consisting of: H, OH, NHR^1, NHacyl, C_{1-15} alkyl, C_{2-15} alkenyl, C_{1-15} alkoxy, CO_2alkyl, C_{2-15} alkynyl, C_{5-10} aryl, and C_{5-10} heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 R^a groups;

each R^a independently represents a member selected from the group consisting of: $R^{3'}$, halo, CF_3, OCF_3, CN, NO_2, , $OR^{3'}$, $S(O)_p$-$R^{3'}$; $N(R^{3'})_2$, $NR^{3'}COR^{3'}$, $NR^{3'}CO_2R^{3'}$, $NR^{3'}CON(R^{3'})_2$, $NR^{3'}SO_2R^{3'}$, $C(O)R^{3'}$, $CO_2R^{3'}$, $CON(R^{3'})_2$, $SO_2N(R^{3'})_2$, $OCON(R^{3'})_2$, and when $R^{3'}$ is present and represents alkyl, alkenyl, alkynyl, aryl or heteroaryl, said alkyl, alkenyl, alkynyl, aryl or heteroaryl group is optionally substituted with 1 to 3 halo, hydroxy, C_{1-3} alkoxy, carboxy or amino groups, and

when at least two R^a groups are present, they may also be taken in combination with any intervening atoms to represent a 4-6 membered ring, said ring containing 0-3 heteroatoms selected from O, $S(O)_p$ and N, and said ring being optionally interrupted by 1-2 -C(O)- groups, and optionally substituted with 1-3 halo, hydroxy, C_{1-6} alkyl or amino groups;

$R^{3'}$ represents H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl;

R^4 represents R^2, -D-R^5 or  ;

D is selected from O, S(O)p ,NR^1 and CR^6R^7;

R^5 is selected from the group consisting of: C_{5-10} aryl and C_{5-10} heteroaryl, said aryl and heteroaryl being optionally substituted with 1 to 3 R^a groups;

Y^2 is selected from the group consisting of: O, $N(C_{1-15})$ alkyl, $N(CO_2)$alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if Y^2 is O and R^3 is CH_3 th n n is 2;

R^8 is optional and is selected from the group consisting of CR^6R^7, O, NR^6 and $S(O)_p$,

and R^6 and R^7 are independently selected from H and C_{1-6} alkyl.

33. A method according to claim 29 wherein the compound has an IC_{50} equal to or less than 10 μM in the hPPARδ binding assay.

34. The method of Claim 30 wherein the compound has an IC_{50} equal to or less than 100 nM in the hPPARδ binding assay.

35. The method of Claim 31 wherein the compound has an IC_{50} equal to or less than 50 nM in the hPPARδ binding assay.

36. The method of Claim 32 wherein the compound has an IC_{50} equal to or less than 10 nM in the hPPARδ binding assay.

37. A method for the treatment or prevention of diabetes diabetic retinopathy and diabetic nephropathy which comprises administering to a diabetic patient an effective amount of a compound of Claim 21 in combination with a sulfonylurea, fibrate, HMG-CoA reductase inhibitor, beta-sitosterol inhibitor, cholesterol acyltransferase inhibitor, biguanides, cholestyramine, angiotensin II antagonist, melinamide, nicotinic acid, fibrinogen receptor antagonists, aspirin, α-glucosidase inhibitors, insulin secretogogue or insulin.

38. A method for halting, preventing or reducing the risk of developing atherosclerosis and related disease events which comprises administering to a patient in need thereof an effective amount of a compound of Claim 22 in combination with a sulfonylurea, fibrate, HMG-CoA reductase inhibitor, beta-sitosterol inhibitor, cholesterol acyltransferase inhibitor, biguanides, cholestyramine, angiotensin II antagonist, melinamide, nicotinic acid, fibrinogen receptor antagonists, aspirin, α-glucosidase inhibitors, insulin secretogogue or insulin.

39. A method according to claim 35 wherein the compound has an IC_{50} equal to or less than 10 μM in the hPPARδ binding assay.

40. The method of Claim 36 wherein the compound has an IC_{50} equal to or less than 100 nM in the hPPARδ binding assay.

41. The method of Claim 37 wherein the compound has an IC_{50} equal to or less than 50 nM in the hPPARδ binding assay.

42. The method of Claim 38 wherein the compound has an IC_{50} equal to or less than 10 nM in the hPPARδ binding assay.

43. A method for the treatment or prevention of obesity which comprises administering to an obese patient an effective amount of a compound of Claim 27 in combination with fenfluramine, dexfenfluramine, phentermine or a β_3 adrenergic receptor agonist.

44. A pharmaceutical composition which is comprised of a compound as described in claim 2 in combination with a carrier.

45. A composition for the treatment of diabetes, diabetic retinopathy, diabetic nephropathy, lowering triglyceride levels or for halting, preventing or reducing the risk of atherosclerosis and related disease events, or for raising high densisty lipoprotein plasma levels, which comprises an inert carrier and an effective amount of a compound of Claim 1.

46. A pharmaceutical composition in accordance with claim 44 which is further comprised of at least one member selected from the group consisting of: a sulfonylurea, fibrate, HMG-CoA reductase inhibitor, beta-sitosterol inhibitor, cholesterol acyltransferase inhibitor, biguanide, cholestyramine, angiotensin II antagonist, melinamide, nicotinic acid, fibrinogen receptor antagonist, aspirin, α-glucosidase inhibitor, insulin secretagogue and insulin.

47. A composition for the treatment of diabetes diabetic retinopathy and diabetic nephropathy which comprises an inert carrier and an effective amount of a compound of Claim 1, in combination with a sulfonylurea, fibrate, HMG-CoA reductase inhibitor, beta-sitosterol inhibitor, cholesterol acyltransferase inhibitor, biguanide, cholestyramine, angiotensin II antagonist, melinamide, nicotinic acid, fibrinogen receptor antagonist, aspirin, α-glucosidase inhibitor, insulin secretagogue or insulin.

48. A composition for halting, preventing or reducing the risk of developing atherosclerosis and related disease events, or for raising high density lipoprotein plasma levels,which comprises an inert carrier and an effective amount of a compound of Claim 1, in combination with a sulfonylurea, fibrate, HMG-CoA reductase inhibitor, beta-sitosterol inhibitor, cholesterol acyltransferase inhibitor, biguanide, cholestyramine, angiotensin II antagonist, melinamide, nicotinic acid, fibrinogen receptor antagonist, aspirin, α-glucosidase inhibitor, insulin secretagogue or insulin.

49. A method according to claim 43 wherein the compound has an IC_{50} equal to or less than 10 μM in the hPPARδ binding assay.

50. The method of Claim 49 wherein the compound has an IC_{50} equal to or less than 50 nM in the hPPARδ binding assay.

51. The method of Claim 50 wherein the compound has an IC_{50} equal to or less than 10 nM in the hPPARδ binding assay.

52. A composition for the treatment of obesity which comprises an inert carrier and an effective amount of a compound of Claim 1, in combination with fenfluramine, dexfenfluramine, phentermine or a β3 adrenergic receptor agonist.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/23646

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 31/135, 31/41, 31/40, 31/395, 31/415, 31/47; C07D 411/02, 413/04, 213/56
US CL :546/164, 175, 271.4, 329, 291, 302, 301, 336, 341

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 546/164, 175, 271.4, 329, 291, 302, 301, 336, 341; 514/402, 379, 646, 342, 866

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE, APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,541,208 A (GARCIA ET AL.) 30 July 1996, Column 7, Lines 49-67.	1-52

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
14 MARCH 1998	27 APR 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer EBENEZER SACKEY Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/23646

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☒ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/23646

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

The following table defines the inventions claimed in this application. By selecting a single variable from each heading, one can arrive at 154 individual groups:

Formula I

A	Y	B
a bond	$S(O_2)$	Furanyl
1 C	$-CH_2-$	Isoxazole
	C=O	Pyrole
	NR^1	Quinoline
	SO_2NH	O Quinazoline
	$NHSO_2$	

Formula Ia

A	Y	Y^2		
a bond	$S(O_2)$	O	NR^1	N-Oalkyl
1 C	$-CH_2-$	$N(C_{1-15})alk$	SO_2NH	N-OH
	C=O	$N(CO_2)alk$		
O	N-Oacyl			

Composition and method claims will be examined as commensurate in scope with the group(s) elected.

A sample selection of an individual group is given below:

Group I, claim 1, drawn to compounds of formula I, wherein A is a bond, Y is $S(O_2)$ and B is furanyl.

The inventions listed as Groups 1-154 do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: no special technical feature which makes a contribution over the prior art is found in all the structural possibilities depicted for formulae I and Ia in claim 1. The disclosed examples, e.g. indole moiety of example 1 is known in the art and, thus , does not make a contribution over the prior art. Therefore, any contribution over the prior art must come from the variable substituents and combinations thereof which are not found in every compound and are not known as equivalents in the art.